SEARCH NOTES 09/939,093 41,4/05

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LOGINID: sssptalar1614

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

Welcome to STN International Web Page URLs for STN Seminar Schedule - N. America NEWS NEWS "Ask CAS" for self-help around the clock CA/CAPLUS - Russian Agency for Patents and Trademarks NEWS 3 FEB 25 (ROSPATENT) added to list of core patent offices covered NEWS 4 FEB 28 PATDPAFULL - New display fields provide for legal status data from INPADOC FEB 28 BABS - Current-awareness alerts (SDIs) available NEWS 5 NEWS 6 FEB 28 MEDLINE/LMEDLINE reloaded MAR 02 GBFULL: New full-text patent database on STN NEWS 7 NEWS 8 MAR 03 REGISTRY/ZREGISTRY - Sequence annotations enhanced MEDLINE file segment of TOXCENTER reloaded NEWS 9 MAR 03 NEWS 10 MAR 22 KOREAPAT now updated monthly; patent information enhanced NEWS 11 MAR 22 Original IDE display format returns to REGISTRY/ZREGISTRY PATDPASPC - New patent database available 12 MAR 22 NEWS NEWS 13 MAR 22 REGISTRY/ZREGISTRY enhanced with experimental property tags NEWS 14 APR 04 EPFULL enhanced with additional patent information and new fields 15 APR 04 EMBASE - Database reloaded and enhanced NEWS JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT NEWS EXPRESS MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005 **NEWS HOURS** STN Operating Hours Plus Help Desk Availability NEWS INTER General Internet Information NEWS LOGIN Welcome Banner and News Items NEWS PHONE Direct Dial and Telecommunication Network Access to STN NEWS WWW CAS World Wide Web Site (general information)

Enter NEWS followed by the item number or name to see news on that specific topic.

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FILE 'HOME' ENTERED AT 12:07:55 ON 14 APR 2005

=> activate

THIS COMMAND NOT AVAILABLE IN THE CURRENT FILE Some commands only work in certain files. For example, the EXPAND command can only be used to look at the index in a file which has an index. Enter "HELP COMMANDS" at an arrow prompt (=>) for a list of commands which can be used in this file.

SEARCH NOTES 09/939,093 4114/805

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
	1	"5622985".pn.	US-PGPUB; USPAT; USOCR			2005/04/14 15:46
L2	20	"1-ethyl-2-benzimidazolinone"	US-PGPUB; USPAT; USOCR	OR	ON	2005/04/14 15:47

=> file caplus COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 161.33 162.89

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 12:58:47 ON 14 APR 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE COVERS 1907 - 14 Apr 2005 VOL 142 ISS 16 FILE LAST UPDATED: 13 Apr 2005 (20050413/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 1101

L102 6484 L101

=> s 1102 and (sexual desire? or sexual arousal? or orgasm? or sexual pain? or dyspareunia? or vaginismus?)

29921 SEXUAL

32 SEXUALS

29940 SEXUAL

(SEXUAL OR SEXUALS)

146242 DESIRE?

150 SEXUAL DESIRE?

(SEXUAL(W) DESIRE?)

29921 SEXUAL

32 SEXUALS

29940 SEXUAL

(SEXUAL OR SEXUALS)

4109 AROUSAL?

260 SEXUAL AROUSAL?

(SEXUAL (W) AROUSAL?)

158 ORGASM?

29921 SEXUAL

32 SEXUALS

29940 SEXUAL

(SEXUAL OR SEXUALS)

128819 PAIN?

13 SEXUAL PAIN?

(SEXUAL (W) PAIN?)

89 DYSPAREUNIA?

14 VAGINISMUS?

L103 2 L102 AND (SEXUAL DESIRE? OR SEXUAL AROUSAL? OR ORGASM? OR SEXUAL PAIN? OR DYSPAREUNIA? OR VAGINISMUS?)

structure-building or screen commands and text search terms. L#s created via the STRUCTURE or SCREEN commands must be searched in the structures files separately from text terms or profiles. The L# answer sets from structure searches can be used in crossover searches and can be combined with text terms.

=> file registry COST IN U.S. DOLLARS

SINCE FILE TOTAL SESSION 1.35 1.56

FULL ESTIMATED COST

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Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 13 APR 2005 HIGHEST RN 848462-79-3 DICTIONARY FILE UPDATES: 13 APR 2005 HIGHEST RN 848462-79-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

=> s 190

SAMPLE SEARCH INITIATED 12:58:29 FILE 'REGISTRY' SAMPLE SCREEN SEARCH COMPLETED - 4148 TO ITERATE

24.1% PROCESSED 1000 ITERATIONS INCOMPLETE SEARCH (SYSTEM LIMIT EXCEEDED) SEARCH TIME: 00.00.01

50 ANSWERS

FULL FILE PROJECTIONS: ONLINE **COMPLETE**

PROJECTED ITERATIONS: 79098 TO 86822 PROJECTED ANSWERS: 11337 TO 14379

L100 50 SEA SSS SAM L90

=> s 190 full FULL SEARCH INITIATED 12:58:38 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 82442 TO ITERATE

100.0% PROCESSED 82442 ITERATIONS SEARCH TIME: 00.00.03

13897 ANSWERS

```
1081) SEA BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBI
           18992) SEA FILE=MEDLINE ABB=ON PLU=ON L24 OR L30
L42 (
L43 (
           12810) SEA FILE=BIOSIS ABB=ON PLU=ON L25 OR L31
L44 (
            4748) SEA FILE=CAPLUS ABB=ON PLU=ON L26 OR L32
L45 (
           22707) SEA FILE=EMBASE ABB=ON PLU=ON L27 OR L33
L46 (
            4173) SEA FILE=WPIDS ABB=ON PLU=ON L28 OR L34
L47 (
           63430) SEA L29 OR L35
           89255) SEA FILE=MEDLINE ABB=ON PLU=ON CLITOR? OR GENITAL? OR SEXUAL
L48 (
           54070) SEA FILE=BIOSIS ABB=ON PLU=ON CLITOR? OR GENITAL? OR SEXUAL G.
L49 (
           12575) SEA FILE=CAPLUS ABB=ON PLU=ON CLITOR? OR GENITAL? OR SEXUAL G
L50 (
          182062) SEA FILE=EMBASE ABB=ON PLU=ON CLITOR? OR GENITAL? OR SEXUAL G
L51 (
L52 (
            5255) SEA FILE=WPIDS ABB=ON PLU=ON CLITOR? OR GENITAL? OR SEXUAL GE
L53 (
          343217) SEA CLITOR? OR GENITAL? OR SEXUAL GENITAL? OR PENIS? OR PENILE?
L54 (
          99793) SEA FILE=MEDLINE ABB=ON PLU=ON L42 OR L48
L55 (
           61673) SEA FILE=BIOSIS ABB=ON PLU=ON L43 OR L49
          15359) SEA FILE=CAPLUS ABB=ON PLU=ON L44 OR L50 195622) SEA FILE=EMBASE ABB=ON PLU=ON L45 OR L51
L56 (
L57 (
L58 (
            8559) SEA FILE=WPIDS ABB=ON PLU=ON L46 OR L52
L59 (
        · 381006) SEA L47 OR L53
L60 (
               1) SEA FILE=MEDLINE ABB=ON PLU=ON L54 AND (L18 OR L36)
               1) SEA FILE=BIOSIS ABB=ON PLU=ON L55 AND (L19 OR L37)
3) SEA FILE=CAPLUS ABB=ON PLU=ON L56 AND (L20 OR L38)
2) SEA FILE=EMBASE ABB=ON PLU=ON L57 AND (L21 OR L39)
L61 (
L62 (
L63 (
               3) SEA FILE=WPIDS ABB=ON PLU=ON L58 AND (L22 OR L40)
L64 (
L65 (
              10) SEA L59 AND (L23 OR L41)
L66 (
               6) DUP REM L65 (4 DUPLICATES REMOVED)
L67 (
             731) SEA FILE=MEDLINE ABB=ON PLU=ON ((INTERMEDIATE CONDUCTANCE) (5
L68 (
            1070) SEA FILE=BIOSIS ABB=ON PLU=ON ((INTERMEDIATE CONDUCTANCE) (5A
            1359) SEA FILE=CAPLUS ABB=ON PLU=ON ((INTERMEDIATE CONDUCTANCE) (5A 220) SEA FILE=EMBASE ABB=ON PLU=ON ((INTERMEDIATE CONDUCTANCE) (5A
L69 (
L70 (
              51) SEA FILE=WPIDS ABB=ON PLU=ON ((INTERMEDIATE CONDUCTANCE) (5A)
L71 ( ·
L72 (
            3431) SEA ((INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?))
L73 (
             821) SEA FILE=MEDLINE ABB=ON PLU=ON L18 OR L36 OR L67
L74 (
            1194) SEA FILE=BIOSIS ABB=ON PLU=ON L19 OR L37 OR L68
            1935)SEA FILE=CAPLUS ABB=ON PLU=ON L20 OR L38 OR L69 347)SEA FILE=EMBASE ABB=ON PLU=ON L21 OR L39 OR L70
L75 (
L76 (
L77 (
             114) SEA FILE-WPIDS ABB=ON PLU=ON L22 OR L40 OR L71
L78 (
            4411) SEA L23 OR L41 OR L72
L79 (
               8) SEA FILE=MEDLINE ABB=ON PLU=ON L54 AND L73
L80 (
               7) SEA FILE=BIOSIS ABB=ON PLU=ON L55 AND L74
L81 (
             12) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                   L56 AND L75
L82 (
               2) SEA FILE=EMBASE ABB=ON PLU=ON L57 AND L76
L83 (
               3) SEA FILE-WPIDS ABB-ON PLU-ON L58 AND L77
L84 (
              32) SEA L59 AND L78
L85 (
             20) DUP REM L84 (12 DUPLICATES REMOVED)
L86 (
            141) SEA FILE=CAPLUS ABB=ON PLU=ON (INTERMEDIATE CONDUCTANCE CALCI
L87 (
            609) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                    BENZIMIDAZOLINONE? OR "1-ETHYL-
L88 (
            1637) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                    ((INTERMEDIATE CONDUCTANCE) (5A
            2210) SEA FILE=CAPLUS ABB=ON PLU=ON L86 OR L87 OR L88
L89 (
L90
                 STR
L91 (
           13897) SEA FILE=REGISTRY SSS FUL L90
L92 (
            6484) SEA FILE=CAPLUS ABB=ON PLU=ON L91
L93 (
                                           PLU=ON L89 AND L92
            194) SEA FILE=CAPLUS ABB=ON
                                            PLU=ON L93 AND (L26 OR L32 OR L50)
L94 (
               0) SEA FILE=CAPLUS ABB=ON
                                            PLU=ON L93 AND (SEX? DYSF?)
L95 (
               0) SEA FILE=CAPLUS ABB=ON
                                            PLU=ON L93 AND (SEXUAL DYSFUNCTION? OR
L96 (
               2) SEA FILE=CAPLUS ABB=ON
L97 (
              20) SEA FILE=CAPLUS ABB=ON PLU=ON L92 AND (L26 OR L32 OR L50)
L98 (
              6) SEA FILE=CAPLUS L85
L99 (
              20) SEA FILE=CAPLUS L97 NOT L98
```

The query entered contains both search terms created by

^{=&}gt; s 192 and (sexual desire? or sexual arousal? or orgasm? or sexual pain? or dyspareunia? or vaginismus?)
COMBINATION OF STRUCTURE AND TEXT TERMS NOT VALID

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FILE COVERS 1907 - 14 Apr 2005 VOL 142 ISS 16 FILE LAST UPDATED: 13 Apr 2005 (20050413/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

```
=> activate
ENTER NAME OF SAVED ITEM TO ACTIVATE OR (END):109939093a/1
L1
                 STR
              50) SEA FILE=REGISTRY SSS SAM L1
L2
L3
               0) SEA FILE=REGISTRY EXA FUL L1
L4
            4907) SEA FILE=REGISTRY SSS FUL L1
L5
             61) SEA FILE=CAPLUS ABB=ON PLU=ON L2
L6
             112) SEA FILE=CAPLUS ABB=ON PLU=ON L2 OR "1-ETHYL-2-BENZIMIDAZOLIN
L7
              1) SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (SEXUAL DYSFUNCTION? OR
L8
                                           PLU=ON L6 AND GENITALIA?
               0) SEA FILE=CAPLUS ABB=ON
               1) SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (SEXUAL?)
L9
L10
                 STR
              50)SEA FILE=REGISTRY SSS SAM L10
L11 (
            4907)SEA FILE=REGISTRY SSS FUL L1
L12 (
L13 (
           13889) SEA FILE=REGISTRY SSS FUL L10
L14 (
              58) SEA FILE=CAPLUS ABB=ON PLU=ON L13 AND (SEXUAL DYSFUNCTION? OR
L15 (
               1) SEA FILE=CAPLUS ABB=ON PLU=ON L14 AND (CALCIUM CHANNEL?)
L16 (
               5) SEA FILE=CAPLUS ABB=ON PLU=ON L14 AND CALCIUM?
L17 (
              53) SEA FILE=CAPLUS ABB=ON PLU=ON L14 NOT (L15 OR L16)
L18 (
             146) SEA FILE=MEDLINE ABB=ON PLU=ON (INTERMEDIATE CONDUCTANCE CALC
L19 (
             154) SEA FILE=BIOSIS ABB=ON PLU=ON (INTERMEDIATE CONDUCTANCE CALCI
L20 (
             141) SEA FILE=CAPLUS ABB=ON PLU=ON (INTERMEDIATE CONDUCTANCE CALCI
L21 (
              29) SEA FILE=EMBASE ABB=ON PLU=ON (INTERMEDIATE CONDUCTANCE CALCI
L22 (
              17) SEA FILE=WPIDS ABB=ON PLU=ON (INTERMEDIATE CONDUCTANCE CALCIU
L23 (
             487) SEA (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANN
L24 (
           18983) SEA FILE=MEDLINE ABB=ON PLU=ON (SEXUAL DYSFUNCTION? OR SEXUAL
L25 (
           12802) SEA FILE=BIOSIS ABB=ON PLU=ON (SEXUAL DYSFUNCTION? OR SEXUAL
L26 (
            4743) SEA FILE=CAPLUS ABB=ON PLU=ON (SEXUAL DYSFUNCTION? OR SEXUAL
           22704) SEA FILE=EMBASE ABB=ON PLU=ON (SEXUAL DYSFUNCTION? OR SEXUAL
L27 (
            4167) SEA FILE-WPIDS ABB-ON PLU-ON (SEXUAL DYSFUNCTION? OR SEXUAL D
L28 (
           63399) SEA (SEXUAL DYSFUNCTION? OR SEXUAL DISFUNCTION? OR ERECTILE DYS
L29 (
L30 (
             255) SEA FILE=MEDLINE ABB=ON PLU=ON (FEMALE SEXUAL DYSFUNCTION? OR
            177) SEA FILE=BIOSIS ABB=ON PLU=ON (FEMALE SEXUAL DYSFUNCTION? OR 200) SEA FILE=CAPLUS ABB=ON PLU=ON (FEMALE SEXUAL DYSFUNCTION? OR 692) SEA FILE=EMBASE ABB=ON PLU=ON (FEMALE SEXUAL DYSFUNCTION? OR
L31 (
L32 (
L33 (
L34 (
             334) SEA FILE=WPIDS ABB=ON PLU=ON (FEMALE SEXUAL DYSFUNCTION? OR F
            1658) SEA (FEMALE SEXUAL DYSFUNCTION? OR FEMALE SEXUAL DISFUNCTION? O
L35 (
L36 (
             112) SEA FILE=MEDLINE ABB=ON PLU=ON BENZIMIDAZOLINONE? OR "1-ETHYL
             159) SEA FILE=BIOSIS ABB=ON PLU=ON BENZIMIDAZOLINONE? OR "1-ETHYL-
L37 (
            609) SEA FILE=CAPLUS ABB=ON PLU=ON BENZIMIDAZOLINONE? OR "1-ETHYL-135) SEA FILE=EMBASE ABB=ON PLU=ON BENZIMIDAZOLINONE? OR "1-ETHYL-
L38 (
L39 (
L40 (
            66) SEA FILE-WPIDS ABB-ON PLU-ON BENZIMIDAZOLINONE? OR "1-ETHYL-2
```

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PASSWORD:

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 NEWS
          FEB 25
                  CA/CAPLUS - Russian Agency for Patents and Trademarks
                  (ROSPATENT) added to list of core patent offices covered
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          FEB 28
                  PATDPAFULL - New display fields provide for legal status
                  data from INPADOC
 NEWS
          FEB 28
                  BABS - Current-awareness alerts (SDIs) available
         FEB 28
 NEWS
                  MEDLINE/LMEDLINE reloaded
      7
         MAR 02
 NEWS
                  GBFULL: New full-text patent database on STN
 NEWS 8
         MAR 03
                  REGISTRY/ZREGISTRY - Sequence annotations enhanced
         MAR 03
 NEWS
                  MEDLINE file segment of TOXCENTER reloaded
NEWS
      10 MAR 22
                  KOREAPAT now updated monthly; patent information enhanced
       11 MAR 22
                  Original IDE display format returns to REGISTRY/ZREGISTRY
 NEWS
       12 MAR 22
                  PATDPASPC - New patent database available
 NEWS
       13 MAR 22
 NEWS
                  REGISTRY/ZREGISTRY enhanced with experimental property tags
 NEWS
      14 APR 04
                  EPFULL enhanced with additional patent information and new
                  fields
 NEWS
      15 APR 04
                  EMBASE - Database reloaded and enhanced
               JANUARY 10 CURRENT WINDOWS VERSION IS V7.01a, CURRENT
 NEWS EXPRESS
               MACINTOSH VERSION IS V6.0c(ENG) AND V6.0jc(JP),
               AND CURRENT DISCOVER FILE IS DATED 10 JANUARY 2005
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               General Internet Information
 NEWS LOGIN
               Welcome Banner and News Items
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Enter NEWS followed by the item number or name to see news on that
```

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FILE 'HOME' ENTERED AT 12:56:43 ON 14 APR 2005

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL
ENTRY SESSION
0.21 0.21

FULL ESTIMATED COST

FILE 'CAPLUS' ENTERED AT 12:56:48 ON 14 APR 2005

```
L3 (
              O)SEA FILE=REGISTRY EXA FUL L1
           4907) SEA FILE=REGISTRY SSS FUL L1
L4
L5
             61) SEA FILE=CAPLUS ABB=ON PLU=ON L2
            112) SEA FILE=CAPLUS ABB=ON PLU=ON L2 OR "1-ETHYL-2-BENZIMIDAZOLIN
L6
L7
              1) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                                L6 AND (SEXUAL DYSFUNCTION? OR
L8
              0) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                                L6 AND GENITALIA?
L9
              1) SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (SEXUAL?)
L10
                STR
L11 (
             50) SEA FILE=REGISTRY SSS SAM L10
L12 (
           4907) SEA FILE=REGISTRY SSS FUL L1
L13 (
          13889) SEA FILE=REGISTRY SSS FUL L10
             58) SEA FILE=CAPLUS ABB=ON PLU=ON L13 AND (SEXUAL DYSFUNCTION? OR
L14 (
L15 (
              1) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON L14 AND (CALCIUM CHANNEL?)
L16 (
              5) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                                L14 AND CALCIUM?
             53) SEA FILE=CAPLUS ABB=ON PLU=ON L14 NOT (L15 OR L16)
L17 (
     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 12:08:44 ON 14
     APR 2005
L18
            487 S (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANNEL
L19
          63399 S (SEXUAL DYSFUNCTION? OR SEXUAL DISFUNCTION? OR ERECTILE DYSFU
          1658 S (FEMALE SEXUAL DYSFUNCTION? OR FEMALE SEXUAL DISFUNCTION? OR
L20
           1081 S BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO"
L21
L22
          63430 S L19 OR L20
L23
         343217 S CLITOR? OR GENITAL? OR SEXUAL GENITAL? OR PENIS? OR PENILE? O
L24
         381006 S L22 OR L23
L25
             10 S L24 AND (L18 OR L21)
L26
              6 DUP REM L25 (4 DUPLICATES REMOVED)
L27
           3431 S ((INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?)) OR
           4411 S L18 OR L21 OR L27
L28
L29
             32 S L24 AND L28
L30
             20 DUP REM L29 (12 DUPLICATES REMOVED)
     FILE 'STNGUIDE' ENTERED AT 12:22:03 ON 14 APR 2005
     FILE 'CAPLUS' ENTERED AT 12:28:09 ON 14 APR 2005
L31
            141 S (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANNEL
            609 S BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO"
L32
           1637 S ((INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?)) OR
L33
L34
           2210 S L31 OR L32 OR L33
     FILE 'REGISTRY' ENTERED AT 12:31:39 ON 14 APR 2005
L35
                STRUCTURE UPLOADED
L36
          13897 S L35 FULL
     FILE 'CAPLUS' ENTERED AT 12:32:08 ON 14 APR 2005
L37
           6484 S L36
L38
            194 S L34 AND L37
              0 S L38 AND (L19 OR L20 OR L23)
L39
L40
              0 S L38 AND (SEX? DYSF?)
              2 S L38 AND (SEXUAL DYSFUNCTION? OR PENIS? OR PENILE? OR ERECTILE
L41
             20 S L37 AND (L19 OR L20 OR L23)
L42
L43
              6 S L30
L44
             20 S L42 NOT L30
```

FILE 'STNGUIDE' ENTERED AT 12:37:33 ON 14 APR 2005 SAVE ALL L09939093A/L

```
L11 (
            50) SEA FILE=REGISTRY SSS SAM L10
L12 (
          4907) SEA FILE=REGISTRY SSS FUL L1
L13 (
          13889) SEA FILE=REGISTRY SSS FUL L10
             58) SEA FILE=CAPLUS ABB=ON PLU=ON L13 AND (SEXUAL DYSFUNCTION? OR
L14 (
L15 (
              1) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON L14 AND (CALCIUM CHANNEL?)
L16 (
              5) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON L14 AND CALCIUM?
L17 (
             53) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON L14 NOT (L15 OR L16)
     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 12:08:44 ON 14
            487 S (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANNEL
L18
L19
          63399 S (SEXUAL DYSFUNCTION? OR SEXUAL DISFUNCTION? OR ERECTILE DYSFU
L20
           1658 S (FEMALE SEXUAL DYSFUNCTION? OR FEMALE SEXUAL DISFUNCTION? OR
           1081 S BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO"
L21
L22
          63430 S L19 OR L20
L23
         343217 S CLITOR? OR GENITAL? OR SEXUAL GENITAL? OR PENIS? OR PENILE? O
L24
         381006 S L22 OR L23
L25
             10 S L24 AND (L18 OR L21)
L26
              6 DUP REM L25 (4 DUPLICATES REMOVED)
L27
           3431 S ((INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?)) OR
L28
           4411 S L18 OR L21 OR L27
L29
             32 S L24 AND L28
L30
             20 DUP REM L29 (12 DUPLICATES REMOVED)
     FILE 'STNGUIDE' ENTERED AT 12:22:03 ON 14 APR 2005
     FILE 'CAPLUS' ENTERED AT 12:28:09 ON 14 APR 2005
            141 S (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANNEL
L31
L32
            609 S BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO"
L33
           1637 S ((INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?)) OR
L34
           2210 S L31 OR L32 OR L33
     FILE 'REGISTRY' ENTERED AT 12:31:39 ON 14 APR 2005
               STRUCTURE UPLOADED
L35
L36
          13897 S L35 FULL
     FILE 'CAPLUS' ENTERED AT 12:32:08 ON 14 APR 2005
L37
           6484 S L36
L38
            194 S L34 AND L37
L39
              0 S L38 AND (L19 OR L20 OR L23)
L40
              0 S L38 AND (SEX? DYSF?)
L41
              2 S L38 AND (SEXUAL DYSFUNCTION? OR PENIS? OR PENILE? OR ERECTILE
L42
             20 S L37 AND (L19 OR L20 OR L23)
L43
             6 S L30
             20 S L42 NOT L30
L44
     FILE 'STNGUIDE' ENTERED AT 12:37:33 ON 14 APR 2005
=> save
ENTER L#, L# RANGE, ALL, OR (END):all
ENTER NAME OR (END):109939093a/1
L# LIST L1-L44 HAS BEEN SAVED AS 'L09939093A/L'
=> d his
     (FILE 'HOME' ENTERED AT 12:07:55 ON 14 APR 2005)
     FILE 'CAPLUS' ENTERED AT 12:08:10 ON 14 APR 2005
               ACTIVATE L09939093/L
               _____
L1
                STR
L2 (
             50) SEA FILE=REGISTRY SSS SAM L1
```

L10

STR

The Nantucket pine tip moth (Rhyacionia frustrana) was accidently introduced on Monterey pine into San Diego, San Bernadino, and Kern Counties, Calif., identification being based on genitalia, wing length, overwintering pupation site, and most probable geographic origin. Very good control was obtained with 4 annual sprays of Zectran (I) [315-18-4], dimethoate [60-51-5], acephate [30560-19-1], trichlorfon [52-68-6], or phosalone [2310-17-0] in 2 different seasons. One season's trial of Imidan [732-11-6] or chlorpyrifos [2921-88-2] sprays gave good control, whereas methoxychlor, diazinon, lindane, or malathion gave mediocre to poor control. One soil application of granular carbofuran [1563-66-2] or aldicarb [116-06-3] gave good control, but granular acephate or disulfoton gave no control.

=> file stnguide		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	90.70	538.98
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-16.06	-21.90

FILE 'STNGUIDE' ENTERED AT 12:37:33 ON 14 APR 2005 USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION. LAST RELOADED: Apr 8, 2005 (20050408/UP).

=> d cost		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
CONNECT CHARGES	0.00	47.67
NETWORK CHARGES	0.48	3.48
SEARCH CHARGES	0.00	382.03
DISPLAY CHARGES	0.00	106.28
FULL ESTIMATED COST	0.48	539.46
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
(ENTRY	SESSION
CA SUBSCRIBER PRICE	0.00	-21.90

IN FILE 'STNGUIDE' AT 12:42:36 ON 14 APR 2005

=> d his

(FILE 'HOME' ENTERED AT 12:07:55 ON 14 APR 2005)

FILE 'CAPLUS' ENTERED AT 12:08:10 ON 14 APR 2005 ACTIVATE L09939093/L

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L1
                 STR
L2
             50) SEA FILE=REGISTRY SSS SAM L1
L3
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L4
           4907) SEA FILE=REGISTRY SSS FUL L1
L5
             61) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                 L2
L6
            112) SEA FILE=CAPLUS ABB=ON
                                          PLU=ON
                                                  L2 OR "1-ETHYL-2-BENZIMIDAZOLIN
L7
              1) SEA FILE=CAPLUS ABB=ON
                                          PLU=ON
                                                  L6 AND (SEXUAL DYSFUNCTION? OR
rs
              0) SEA FILE=CAPLUS ABB=ON
                                          PLU=ON
                                                  L6 AND GENITALIA?
L9
              1) SEA FILE=CAPLUS ABB=ON
                                          PLU=ON
                                                 L6 AND (SEXUAL?)
```

optionally substituted Ph, naphthyl, or heteroaryl; R6 = H, C1-6 alkyl, each optionally substituted Ph, naphthyl, heteroaryl, or phenyl-C1-6 alkyl, CO2R8 (where R8 is an ester group); m, p = 0-4; n = 1-4; Z = NR9, O, S, CR9R10; R9, R10 = H, C1-6 alkyl, optionally substituted phenyl-C1-6 alkyl; X = O, S; Y = Q, Q1 (where R11, R12 = H, C1-6 alkyl, CF3, each optionally substituted Ph, naphthyl, or heteroaryl)] and salts and solvates thereof, which are useful for the treatment of diseases of central nervous system such as obesity, bulimia, alcoholism, pain, depression, hypertension, aging, memory loss, sexual dysfunction, anxiety, schizophrenia, gastrointestinal disorders, headache, cardiovascular disorders, smoking cessation, drug addiction, and emėsis, are prepared Thus, 8.7 mmol 1-[2-(1,2,3,4-tetrahydro-9H-pyrido[3,4b]indol-2-yl)-1-ethyl]-1,3-dihydrobenzimidazol-2-one was suspended in 50 mL Me iso-Bu ketone, treated with 9.58 mmol 1-(2-chloroethyl)-1,3-dihydro-2H-benzimidazol-2-one, 10.45 mmol Na2CO3, and 10 mg Bu4NI, and the suspension was heated to 90° for 2 days to give the title compound (II). A total of 23 I were prepared and showed binding affinity to $5-HT1D\alpha$ receptor with Ki values 20-5,000 nM and also possessed binding activity at the 5-HT1D\$\beta\$ and 5-HT2A receptors.

L42 ANSWER 19 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1989:51232 CAPLUS

DOCUMENT NUMBER: 110:51232

TITLE: Apomorphine and haloperidol, but not domperidone,

affect penile reflexes in rats

Pehek, Elizabeth A.; Thompson, James T.; Eaton, Robert C.; Bazzett, Terence J.; Hull, Elaine M. AUTHOR (S):

CORPORATE SOURCE: Dep. Psychol., State Univ. New York, Buffalo, NY,

14260, USA

SOURCE: Pharmacology, Biochemistry and Behavior (1988), 31(1),

CODEN: PBBHAU; ISSN: 0091-3057

DOCUMENT TYPE: Journal LANGUAGE: English ED Entered STN: 17 Feb 1989

AB Systemic administration of the dopamine agonist apomorphine produces a biphasic effect on erection in freely moving rats, with lower doses facilitating, and high doses inhibiting, erection. However, these studies did not distinguish between erection per se and seminal emission. Apomorphine produced a similar biphasic effect on penile reflexes in the restrained, supine rat, while facilitating seminal emission in a monophasic fashion. Haloperidol, a centrally-acting dopamine antagonist, either blocked the effects produced by apomorphine administration, or had actions opposite to those of apomorphine. Domperidone, a dopamine antagonist that does not readily penetrate the blood-brain barrier, did not antagonize apomorphine's effects, and did not affect penile responses when administered alone. Thus, dopamine receptors in the central nervous system regulate genital responses, and the effects on penile reflexes and seminal emission can be exptl. dissociated

L42 ANSWER 20 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1975:492329 CAPLUS

DOCUMENT NUMBER: 83:92329

TITLE: Nantucket pine tip moth in southern California.

Identity and insecticidal control

AUTHOR(S): Brown, Leland R.; Eads, Clark O.

CORPORATE SOURCE: Dep. Entomol., Univ. California, Riverside, CA, USA SOURCE: Journal of Economic Entomology (1975), 68(3), 380-2

CODEN: JEENAI; ISSN: 0022-0493

DOCUMENT TYPE: Journal LANGUAGE: English ED Entered STN: 12 May 1984

GI For diagram(s), see printed CA Issue.

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CA 2157998	AA	19960313	CA 1995-2157998	19950911
US 5563147	A	19961008	US 1995-462237	19950605
EP 705832	A1	19960410	EP 1995-306253	19950907
EP 705832	B1	20030813		
R: AT, BE, CH,	DE, DK	, ES, FR,	GB, GR, IE, IT, LI, LU,	NL, PT, SE
AT 247114	E	20030815	AT 1995-306253	
ES 2204932	Т3	20040501		
AU 9530497	A1	19960328	AU 1995-30497	19950908
AU 698580	B2	19981105		
ни 72593	A2	19960528	HU 1995-2631	19950908
HU 219491	В	20010428		
CZ 286565	В6	20000517	CZ 1995-2322	19950908
FI 9504243	Α	19960313	FI 1995-4243	19950911
NO 9503575	A	19960313	NO 1995-3575	19950911
JP 08081464	A2	19960326	JP 1995-231873	19950911
ZA 9507607	A	19960517	ZA 1995-7607	19950911
CN 1129219	A	19960821	CN 1995-117133	19950911
CN 1045602	В	19991013		
IN 179550	A	19971018	IN 1995-CA1079	19950911
IL 115236	A1	19980615	IL 1995-115236	19950911
RU 2146256	C1	20000310	RU 1995-115522	19950911
PRIORITY APPLN. INFO.:			GB 1994-18326	A 19940912
			GB 1995-11166	A 19950602
OTHER SOURCE(S):	MARPAT	125:33651		4

ER SOURCE(S):

Entered STN: 27 Jun 1996

GI

Pharmaceutical compds. of the formula [I; R1, R7 = halo, CF3, C1-6 alkyl, C1-6 alkoxy, each optionally substituted Ph, naphthyl, or heteroaryl; R2, R3 = H or C1-6 alkyl; R4, R5 = H, halo, CF3, C1-6 alkyl, C1-6 alkoxy, each AΒ

JP 1997-524201 A 19961227 WO 1996-JP3858 W 19961227 US 1998-91997 A1 19981102

OTHER SOURCE(S): MARPAT 127:135799

ED Entered STN: 31 Jul 1997

GΙ

$$R^3$$
 R^3
 R^3
 R^2
 R^2
 R^2
 R^2
 R^3

$$\begin{array}{c|c} X & & \\ & & \\ N & \\ & & \\ C1 & II \end{array}$$

The title compds. [I; R1 = H, arylsulfonyl, (un)substituted lower alkyl, AB etc.; R2 = H, lower cycloalkyl, alkylthio, or alkoxy, OH, SH, NH2, aryl, etc.; R3 = CO2H, NH2, CONH, etc.; R = substituting group or H; m = 1-3] are prepared I, possessing hypoglycemic or PDE5 inhibitory effects, are useful as remedies for impaired glucose tolerance, diabetes, complications of diabetes, insulin resistant syndrome, hyperlipidemia, atherosclerosis, cardiovascular diseases, hyperglycemia, hypertension, angina pectoris, pulmonary hypertension, congestive heart failure, glomerular diseases, tubular interstitial diseases, renal failure, angiostenosis, peripheral vascular disease, apoplexy, chronic reversible obstructive diseases, allergic rhinitis, urticaria, glaucoma, diseases characterized by abnormality in intestinal motility, sexual impotence, nephritis, cancerous cachexia, and post-PCTA reconstriction. Thus, benzimidazole derivative (II; X = OH) was reacted with C6H5SO2NH2 in the presence of N,N'-carbonyldiimidazole and diazabicycloundecene in DMF at 100° for 70 h to give the title compound II (X = PhSO2NH), which showed 72% blood sugar lowering activity when tested with mouse.

L42 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1996:371513 CAPLUS

DOCUMENT NUMBER:

125:33651

TITLE:

Preparation of [(tetrahydropyridoindolyl)alkyl]benzazo

linone derivatives having serotonin $5-HT1D\alpha$

receptor activity

INVENTOR(S):

Gilmore, Jeremy; Gallagher, Peter Thaddeus; Miles, Martin Victor; Owton, William Martin; Smith, Colin

William

PATENT ASSIGNEE(S):

Lilly Industries Ltd., UK Can. Pat. Appl., 34 pp.

CODEN: CPXXEB

DOCUMENT TYPE:

Patent

LANGUAGE:

SOURCE:

English

FAMILY ACC. NUM. COUNT:

': 1

SK 283301	В6	20030502	SK	1999-972		19980116
RU 2204413	C2	20030520	RU	1999-117926		19980116
US 2001018069	A1	20010830	US	1999-352515		19990712
US 6342246	B2	20020129				
MX 9906585	A	20000630	MX	1999-6585		19990714
NO 9903520	А	19990916	NO	1999-3520		19990716
US 2002156056	A1 ·	20021024	US	2001-26492		20011224
PRIORITY APPLN. INFO	.:		GB	1997-878	A	19970117
			WO	1998-GB143	W	19980116
			US	1999-352515	A1	19990712

ED Entered STN: 17 Aug 1998

AB A pharmaceutical composition for oral administration comprises carrier and active ingredient selected from a dopamine agonist, testosterone and mixts. thereof and the composition is in the form of a fast-dispersing dosage form designed to release the active ingredient rapidly in the oral cavity for the manufacture of a medicament for treatment of male erectile dysfunction. A mixture containing gelatin 0.792, mannitol 0.594, apomorphine HCl 0.36, citric acid 0.16632, and purified water 16.8768 kg was dosed into each one of a series of preformed blister pockets and freeze-dried to give an oral unit containing 10 mg apomorphine HCl.

REFERENCE COUNT:

9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

1997:476314 CAPLUS

DOCUMENT NUMBER:

INVENTOR(S):

127:135799

TITLE:

Preparation of benzimidazole derivatives as drugs

Yamasaki, Noritsugu; Imoto, Takafumi; Murai,

Yoshiyuki; Hiramura, Takahiro; Oku, Teruo; Sawada,

Kouzou

PATENT ASSIGNEE(S): SOURCE:

Fujisawa Pharmaceutical Co., Ltd., Japan

PCT Int. Appl., 380 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

Japanese

FAMILY ACC. NUM. COUNT: 2

PA'	PATENT NO.				KIND DATE				APPLICATION NO.						DATE			
WO	97243	34			A1	-	 1997	0710	1	WO	- 1996-	JP38	 58		1	9961	 227	
	W:	AU,	BR,	CA,	CN,	HU,	IL,	JP,	KR,	MX	, NZ,	RU,	SG,	TR,	US,	AM,	AZ,	
					MD,													
	RW:	ΑT,	BE,	CH,	DE,	DK,	ES,	FI,	FR,	GB	, GR,	IE,	ΙΤ,	LU,	MC,	NL,	PT,	SE
CA	22411	86			AΑ		1997	0628	(CA	1996-	2241	186		1	9961	227	
AU	97120	95			A1		1997	0728		ΑU	1997-	1209	5		1	9961:	227	
AU	72251	4			В2		2000	0803										
EP	88271	8			A 1		1998	1209]	EΡ	1996-	9433	31		1	9961	227	
											, IT,							
		ΙE,									•	•	•	•	•	•	,	
CN	12112	38			Α		1999	0317	(CN	1996-	1801	37		1	9961	227	
BR	96124	34			Α		1999	1228			1996-							
JP	20001	5974	19		A2		2000	0613			2000-							
JP	30631	62			B2		2000	0712	,	JP	1997-	5242	01		1	9961	227	
NZ	32483	4			Α		2001	1130			1996-							
IL	12496	9			A1		2002	0912			1996-							
ZA	96109	18			Α		1997	0708			1996-							
TW	54827	2			В		2003	0821			1997-							
ZA	97089	98			Α		1998	0420			1997-					9971		
US	61662	19			Α		2000	1226	I	US	1998-	9199	7			9981		
US	63529	85			В1		2002	0305			2000-							
PRIORIT	Y APPL	N. I	NFO	. :							1995-							
											1996-					9961		

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BR 9916114
                                20030114
                                            BR 1999-16114
                                                                   19991213
    JP 2003521462
                                20030715
                                            JP 2000-587777
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                                                                   19991213
    NZ 511790
                                20040430
                                            NZ 1999-511790
                          Α
                                                                   19991213
    TW 577740
                                            TW 1999-88122257
                                20040301
                         В
                                                                   20000111
     ZA 2001004146
                                20020821
                                            ZA 2001-4146
                         Α
                                                                   20010521
    NO 2001002985
                         Α
                                20010816
                                            NO 2001-2985
                                                                   20010615
                                            BG 2001-105664
    BG 105664
                          Α
                                20020228
                                                                   20010703
PRIORITY APPLN. INFO.:
                                            US 1998-213567
                                                                Α
                                                                   19981217
                                            WO 1999-US29449
                                                                W 19991213
```

ED Entered STN: 23 Jun 2000

AB A method of treating organic erectile dysfunction, particularly vasculogenic erectile dysfunction

comprises administering to a male in need of such treatment a therapeutically effective amount of apomorphine or a pharmaceutically acceptable salt or pro-drug thereof. The apomorphine may be coadministered with an antiemetic agent. A sublingual tablet contained apomorphine hydrochloride 5, ascorbic acid 5, mannitol 67.9, Mg stearate 1, nicotine 1, β -cyclodextrin 20, and D&C Yellow aluminum lake 0.1 mg.

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 1998:509104 CAPLUS

DOCUMENT NUMBER:

129:140693

TITLE:

Dosage forms and method for ameliorating male

erectile dysfunction

INVENTOR(S):

Johnson, Edward Stewart; Clarke, Anthony; Green,

Richard David

PATENT ASSIGNEE(S):

R.P. Scherer Ltd., UK PCT Int. Appl., 31 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PA	CENT	NO.			KIN)	DATE	E APPLICATION NO.						DATE			
						-										 -	
WO	9831																
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											IL,						
											MG,						
		PL,	PT,	RO,	RU,	SD,	SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	UA,	ŪG,
											ΚZ,						
	RW:										AT,						
		FR,	GB,	GR,	ΙE,	ΙT,	LU,	MC,	NL,	PT,	SE,	BF,	ВJ,	CF,	CG,	CI,	CM,
		GA,					SN,										
CA	2276				AA		1998	0723		CA 1	998-	2276	758		1:	9980:	116
	9856	710			A1		1998	0807		AU 1	998-	5671	0		1:	9980	116
	7173																
EΡ	9543	14			A1		1999	1110		EP 1	998-	9009	02		1:	9980	116
ΕP	9543	14			В1		2002	0102									
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,
		ΙE,	LT,	LV,	FI,	RO											
TR	9901	669			Т2		2000	0721	1	TR 1	999-	9901	669		1	9980	116
NZ	3364	36			Α		2000	0728		NZ 1	998-	3364	36		1:	9980	116
	9808				Α		2000	1003			998-				_	9980	116
JΡ	2000	5137	36		Т2		2000	1017		JP 1	998-	5339	51		1:	9980	116
ΑT	2113				E		2002	0115		AT 1	998-	9009	02		1:	9980	116
ES	2167	061			Т3		2002	0501		ES 1	998-	9009	02		1	9980	116
PT	9543	14			Т		2002	0628		PT 1	998-	9009	02		1	9980	116
EE	3805				В1		2002	0815		EE 1	999-	288			1	9980	116
EE	9900	288			Α		2000	0215									

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             CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID,
             IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV,
             MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG,
             SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW,
             AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
         RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE,
             DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF,
             CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG
PRIORITY APPLN. INFO.:
                                            US 1999-123920P
                                                                P 19990312
OTHER SOURCE(S):
                         MARPAT 133:256811
ED
     Entered STN: 22 Sep 2000
AΒ
     The present invention is directed to novel compns. comprising at least one
     dopamine agonist in combination with at least one nitric oxide donor (i.e.
     compds. that donate, transfer or release nitric oxide, elevate endogenous
     levels of endothelium-derived relaxing factor, stimulate endogenous
     synthesis of nitric oxide or are substrates for nitric oxide synthase).
     The novel compns. may optionally comprise at least one therapeutic agent,
     such as, a vasoactive agent, an antiemetic agent, and mixts. thereof. The
     dopamine agonist is preferably apomorphine. The present invention is also
     directed to methods for treating and/or preventing sexual
     dysfunctions and/or enhancing sexual responses in patients.
     other embodiments, the present invention is directed to methods treating
     or preventing neurodegenerative diseases, mitochondrial diseases, spinal
     cord injury, central or psychostimulant addiction, senile dementia,
     circulatory disorders, cardiovascular disorders, hyperprolactinemia or
    myopia. The compds. and/or compns. of the present invention can also be
     provided in the form of a pharmaceutical kit (no data).
REFERENCE COUNT:
                               THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
L42 ANSWER 15 OF 20
                     CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER:
                         2000:420967 CAPLUS
DOCUMENT NUMBER:
                         133:48900
TITLE:
                         Use of apomorphine in the manufacture of a medicament
                         for the treatment of organic erectile
                         dysfunction in males
INVENTOR(S):
                         Kling, Karen; Perdok, Renee J.; Ruff, Dustin D.
PATENT ASSIGNEE(S):
                         Abbott Laboratories, USA
SOURCE:
                         PCT Int. Appl., 23 pp.
                         CODEN: PIXXD2
DOCUMENT TYPE:
                         Patent
LANGUAGE:
                         English
FAMILY ACC. NUM. COUNT:
PATENT INFORMATION:
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PATENT	NO.			KIN	D	DATE APPLICATION NO.							DATE				
WO 2000	0354	57		A1	20000622			WO 1999-US29449						1	9991:	213	
W:	ΑE,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	CA,	CH,	CN,	CR,	CU,	
	CZ,	DE,	DK,	DM,	EE,	ES,	FI,	GB,	GD,	GE,	GH,	GM,	HR,	HU,	ID,	IL,	
						KΡ,											
						MX,											
	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	UZ,	VN,	YU,	ZA,	ZW,	AM,	ΑZ,	
	•		•			ТJ,											
RW:						SD,											
						GR,							SE,	BF,	ВJ,	CF,	
						GW,											
US 6291	471			В1		2001	0918	1	US 1	998-	2135	67		19	9981:	217	
CA 2354															9991:		
EP 1140																	
R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,	
	•	-	FI,														
TR 2001	0171	9		Т2		2002	0821		TR 2	001-	2001	0171	9	19	9991	213	

substituted by hydroxy, lower alkoxy or lower-alkoxy-substituted aralkyl; or two of R3a, R4a and R5a may combine together to form a lower alkylenedioxy. M = 1, 2, provided that when R3a = H, R4a = lower alkoxyand R5a = H, halogen, cyano, lower alkyl, lower alkoxy, protected carboxy, carboxy or nitro, then (1) the lower alkyl for R2a has 1-3 substituents = OH, protected OH, acyl, lower-alkoxy-substituted aralkyloxy, amino, acylamino, lower alkoxycarbonylamino, lower alkanesulfonylamino, ureido, lower alkylureido, sulfamoylamino, protected carboxy, carboxy, lower alkanesulfonyl, lower alkylenedioxy, carbamoyl, lower alkyl carbamoyl and sulfamoyl, (2) the cycloalkyl for R2a has 1-3 substituents = OH, protected OH, acyl, lower-alkoxy-substituted aralkyloxy, amino, acylamino, lower alkoxycarbonylamino, lower alkanesulfonylamino, ureido, lower alkylureido, sulfamoylamino, protected carboxy, lower alkanesulfonyl, lower alkyl, hydroxy(lower)alkyl, protected hydroxy(lower)alkyl, lower alkylenedioxy, carbamoyl and sulfamoyl, (3) the heterocyclic group for R2a = pyrrolidinyl, dioxanyl and piperidyl which groups may be substituted with protected carboxy, acyl, lower alkanesulfonyl, carbamoyl or sulfamoyl, (4) Rla = carbamoyl, lower alkylcarbamoyl which may be substituted with a heterocyclic group, carboxy, protected carboxy, acyl, or lower alkanesulfonyl, (5) Xa = N; (6) m = 2; or (7) yra = S. Pharmaceutical compns. containing the above compds. are claimed (with test data provided for 8 compds.) to be effective for treatment or prevention of diseases mediated by cGMP-PDE: angina, hypertension, pulmonary hypertension, congestive heart failure, glomerular diseases, renal tubulo-intestinal diseases, renal failure, atherosclerosis, conditions of reduced blood vessel patency, peripheral vascular disease, stroke, bronchitis, asthma, allergic rhinitis, urticaria, glaucoma, diseases characterized by disorders of gut motility, erectile dysfunction,

female sexual dysfunction, impotence

, diabetic complications, micturition disorder, or incontinence and storage of urine disorder. The method of preparation comprises reacting II with III (Z1 = halogen) in the presence of base. III are made by intramol. cyclization of IV (X = N). For example, to a solution of 1-(trans-4-hydroxycyclohexyl)-5-trifluoromethyl-2,3-dihydro-1H-benzimidazol-2-one (200 mg) in anhydrous DMF (2 mL) was added portionwise NaH (29.3 mg, 60% dispersion in mineral oil) at 5° under N2 atmosphere, and the mixture was stirred at room temperature for 30 min. After adding 3,4-dimethoxybenzyl bromide (154 mg), the mixture was stirred at room temperature

for 2 h. After workup, 3-(3,4-dimethoxybenzyl)-1-(trans-4-hydroxycyclohexyl)-5-trifluoromethyl-2,3-dihydro-1H-benzimidazol-2-one (217.9 mg) was obtained as a colorless solid.

REFERENCE COUNT:

THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2000:666601 CAPLUS

DOCUMENT NUMBER:

133:256811

TITLE:

Pharmaceutical compositions containing dopamine agonists in combination with nitric oxide donors for

treating and/or preventing sexual

dysfunctions

INVENTOR(S):
PATENT ASSIGNEE(S):

Garvey, David S. Nitromed, Inc., USA PCT Int. Appl., 48 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

SOURCE:

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

IE, SI, LT,	LV,	FI, RO			
TR 200200161	Т2	20020521	TR 2002-200200161		20000712
BR 2000013041	Α	20020716	BR 2000-13041		20000712
JP 2003505376	T2	20030212	JP 2001-511431		20000712
ZA 2002000029	Α	20030402	ZA 2002-29		20020102
US 6582351	В1	20030624	US 2002-30979		20020116
PRIORITY APPLN. INFO.:			AU 1999-1747	Α	19990721
			AU 1999-2730	Α	19990909
			WO 2000-JP4687	W	20000712

OTHER SOURCE(S): MARPAT 134:100871

ED Entered STN: 26 Jan 2001

GΙ

AB Benzimidazolone derivs. I, its prodrugs or pharmaceutically acceptable salts thereof, a method for their preparation, pharmaceutical compns. containing

them, and usefulness in treatment or prevention of diseases mediated by cyclic guanosine-3',5'-monophosphate phosphodiesterase (cGMP-PDE) are claimed. In I, Xa = CH or N; ya = O, S; R1a = halogen, cyano, NO2 carbamoyl, lower alkylcarbamoyl which may be substituted with a heterocyclic group, carboxy, protected carboxy, lower alkyl, halo(lower)alkyl, lower alkoxy, acyl, lower alkanesulfonyl. R2a = lower alkyl, cycloalkyl or heterocyclic group, among which the lower alkyl group may have 1-3 substituents = OH, protected OH, acyl, lower-alkoxysubstituted aralkyloxy, amino, lower alkylamino, acylamino, lower alkoxycarbonylamino, lower alkanesulfonylamino, ureido, lower alkylureido, sulfamoylamino, protected carboxy, carboxy, lower alkanesulfonyl, lower alkylenedioxy, carbamoyl, lower alkyl carbamoyl and sulfamoyl; and the cycloalkyl group and the heterocyclic group may have 1-3 substituents = OH, protected OH, acyl, lower-alkoxy-substituted aralkyloxy, amino, acylamino, lower alkoxycarbonylamino, lower alkanesulfonylamino, ureido, lower alkylureido, sulfamoylamino, protected carboxy, lower alkanesulfonyl, lower alkyl, hydroxy(lower)alkyl, protected hydroxy(lower)alkyl, lower alkylenedioxy, carbamoyl and sulfamoyl. R3a, R4a and R5a = same or different, H, halogen, lower alkanoyl, carboxy, protected carboxy, carbamoyl, nitro, cyano, lower alkyl optionally

BEST AVAILABLE COPY

DOCUMENT NUMBER:

136:288767

TITLE:

Relaxant effects of some benzothiazolinone derivatives

on isolated rabbit corpus cavernosum

AUTHOR(S):

Yildirim, S.; Simsek, R.; Ayan, S.; Gokce, G.; Sarioglu, Y.; Safak, C.

CORPORATE SOURCE:

Cumhuriyet Universitesi, Tip Fak. Farmakoloji ve

Uroloji Anabilim Dali, Sivas, 58140, Turk.

SOURCE:

Urological Research (2001), 29(3), 182-185

CODEN: URLRA5; ISSN: 0300-5623

PUBLISHER:

Springer-Verlag

DOCUMENT TYPE:

Journal

LANGUAGE:

English

Entered STN: 08 Aug 2001

AB In the present study, two 6-(fluorobenzoyl)-3-piperazinomethyl-2benzothiazolinone derivs. were synthesized and their relaxant effects on isolated rabbit corpus cavernosum investigated. Compds. Y-16 and Y-21 can alter the ability of corpus cavernosum smooth muscle to contract. Strips of rabbit corpus cavernosum smooth muscle were mounted in isolated

tissue baths for measurement of isometric contractile force. Compds. (10-6-10-3 M) did not cause contraction but induced relaxation in

precontracted corpus cavernosum smooth muscle.

Neither N-nitro-L-arginine methylester (L-NAME) nor indomethacin affected the relaxant effect of these compds. Glibenclamide and tetraethylammonium chloride (TEA) also did not influence the relaxation induced by the compds. In conclusion, in isolated rabbit corpus cavenosum, Y16 and Y21 have a relaxant potency equal or superior to known vasoactive agents. Further investigations are needed to show the importance of these effects for the diagnosis and treatment of erectile dysfunction

REFERENCE COUNT:

22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2001:63979 CAPLUS

DOCUMENT NUMBER:

134:100871

TITLE:

SOURCE:

Benzimidazolone derivatives, method of preparation and

their use as phosphodiesterase inhibitors

INVENTOR(S):

Sawada, Kozo; Inoue, Takayuki; Sawada, Yuki; Mizutani,

Tsuyoshi

PATENT ASSIGNEE(S):

Fujisawa Pharmaceutical Co., Ltd., Japan

PCT Int. Appl., 159 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PA:	rent	NO.			KIN	D	DATE			APPL:	ICAT	ION :	NO.		D	ATE	
WO	2001	0057	70		A1	_	2001	0125	,	WO 2	000-	JP46	 87		21	0000	 712
	W:									BB,							
										ES,							
		ΗU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KR,	KZ,	LC,	LK,	LR,	LS,	LT,	LU,
		LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NO,	ΝZ,	PL,	PT,	RO,	RU,	SD,
		SE,	SG,	SI,	SK,	SL,	ТJ,	TM,	TR,	TT,	TZ,	UA,	UG,	US,	UZ,	VN,	YU,
		-	•		•	•	•	•	•	RU,	•						
	RW:	GH,															
										IT,					SE,	BF,	ВJ,
										MR,							
	2379									CA 2		_			_	0000	712
	2000															0000	712
EΡ	1196															0000	
	R:	ΑT,	ΒE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	LI,	LU,	NL,	SE,	MC,	PT,

ACCESSION NUMBER:

2002:505409 CAPLUS

DOCUMENT NUMBER:

137:57597

TITLE:

Treatment of antidepressant drug-induced

sexual dysfunction with apomorphine Ruff, Dustin D.; Perdok, Renee J.

INVENTOR(S):

PATENT ASSIGNEE(S): USA

SOURCE:

U.S. Pat. Appl. Publ., 6 pp., Cont. of U. S. Ser. No.

713,741, abandoned.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002086876	A1	20020704	US 2001-974136	20011010
PRIORITY APPLN. INFO.:			US 2000-713741 B1	20001115

ED Entered STN: 05 Jul 2002

A method for treating sexual dysfunction in a patient taking antidepressant medication in need of such treatment comprises administering a therapeutically effective amount of apomorphine or a pharmaceutically acceptable salt thereof. The method may be used for patients taking antidepressants such as tricyclic antidepressants, monamine oxidase inhibitors, or serotonin selective reuptake inhibitors.

L42 ANSWER 11 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2001:868184 CAPLUS

DOCUMENT NUMBER:

136:11136

TITLE:

Rapidly disintegrating tablets

INVENTOR(S):

Lee, Chang Hyun; Woo, Jong Soo; Chang, Hee Chul

PATENT ASSIGNEE(S):

Hanmi Pharm. Co., Ltd., S. Korea PCT Int. Appl., 21 pp.

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

	PATENT NO.					KIND DATE			APPLICATION NO.						DATE				
	WO 2001089485 W: CN, JP					A1	A1 20011129 WO 2001-KR8							93 20010526					
			AT,			ĊY,	DE,	DK,	ES,	FI,	FR,	GB,	GR,	IE,	IT,	LU,	MC,	NL,	
	ΕP	1283	703	•		A1		2003	0219		EP 2	001-	9346	02		2	0010	526	
		R:	-	-				ES, RO,				•	LI,	LU,	NL,	SE,	MC,	PT,	
	JP	2003			21,		/	2003					5857	30		2	0010	526	
PRIO	RITY	' APP	LN.	INFO	.:						KR 2	000-	2866	7	7	A 2	0000	526	
										,	WO 2	001-	KR89	3 .	Ţ	√ 2	0010	526	

ED Entered STN: 30 Nov 2001

A tablet having an enhanced strength as well as a high disintegrating rate in the oral cavity was prepared by mixing a drug a sublimable substance suitable for oral administration and an additive, tableting the mixture, and drying the resulting tablet to sublime the sublimable substance until the tablet becomes porous. Thus, tablets contained ondansetron 8, xanthan gum 6, menthol 29, mannitol 104.4, PEG-3000 9.5, stevioside 5.5, crosslinked PVP 4, Mg stearate 1.2, and SiO2 0.65%.

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 12 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN ACCESSION NUMBER: 2001:571333 CAPLUS

3

US 1995-546498 A2 19951020
US 1998-102406 A1 19980622
US 2000-606919 A2 20000629
EP 1995-916467 A3 19950421
US 2001-44588 A 20011023
WO 2002-US33480 W 20021021

ED Entered STN: 18 Apr 2003

AB Impotence can be ameliorated without substantial undesirable side effects by nasal administration of apomorphine, optionally with an antiemetic agent present in an amount sufficient to substantially reduce nausea symptoms that may be associated with the use of apomorphine. Tablets were prepared from apomorphine-HCl-nicotine combination granulates.

L42 ANSWER 9 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2002:638290 CAPLUS

DOCUMENT NUMBER:

137:163826

TITLE:

Treatment of antidepressant-induced sexual

dysfunction with apomorphine

INVENTOR(S):

Ruff, Dustin D.; Perdok, Renee J.

PATENT ASSIGNEE(S): USA

SOURCE:

U.S. Pat. Appl. Publ., 6 pp.

CODEN: USXXCO

DOCUMENT TYPE:

LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

· P	ATENT	NO.			KIN	D -	DATE			APP	LICAT	ION	NO.		D	ATE			
U: U:	S 2002 S 6528				A1 B2		2002 2003	0822		US 2	2001-	9937	82		2	0011	- 114		
	A 2429				AA			0523	_							20011114			
W	2002	0398	79					0523			2001-								
	2002				A3		2002					00.0	,,,		_	0011	117		
				AL,	AM,	AT,	AU,	AZ.	BA.	BB.	, BG,	BR.	BY.	BZ.	CA.	CH.	CN.		
		co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EE	, ES,	FI,	GB.	GD,	GE.	GH.	GM.		
		HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG	, KP,	KR.	KZ.	LC.	LK.	I.R.	LS.		
		LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW	, MX,	MZ,	NO.	NZ.	PL.	PT.	RO.		
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			YU,				•				,	·		•		,	,		
	RW:	GH,	GM,	ΚE,	LS,	MW,	MZ,	SD,	SL,	SZ	, TZ,	UG,	ZW,	AM,	AZ,	BY,	KG,		
		ΚZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	CH,	CY	, DE,	DK,	ES,	FI,	FR,	GB,	GR.		
		ΙE,	ΙT,	LU,	MC,	NL,	PT,	SE,	TR,	BF,	, BJ,	CF,	CG,	CI,	CM,	GA,	GN,		
		GQ,	GW,	ML,	MR,	NE,	SN,	TD,	TG										
	J 2002																		
E	P 1341	536			A2		2003	0910		EP 2	2001-	9854	80		2	0011	114		
	R:	AT,	BE,	CH,	DE,	DK,	ES,	FR,	GB,	GR,	, IT,	LI,	LU,	NL,	SE,	MC,	PT,		
		ΙE,	SI,	LT,	LV,	FΙ,	RO,	MK,	CY,	AL,	, TR						•		
BI	R 2001	0119	32		Α		2003	1028		BR 2	2001-3	1198	2		2	0011	114		
J1	2004	5138	99		Т2		2004	0513		JP 2	2002-5	5422	5 <i>7</i> .		2	0011	114		
\mathbf{z}_{i}	A 2003 D 2003	0034	71		Α		2004	0806		ZA 2	2003-3	3471			2	0030	506		
																0030	514		
	G 1078	_			Α		2004	0130			2003-1					0030	604		
PRIORI'	RIORITY APPLN. INFO.:									US 2	2000-2	2490	31P	I	2	0001	115		
				_					1	WO 2	2001 - 0	JS439	933	V	V 2	0011	114		

ED Entered STN: 23 Aug 2002

AB A method for treating sexual dysfunction in a patient taking antidepressant medication in need of such treatment comprises administering a therapeutically effective amount of apomorphine, or a pharmaceutically acceptable salt thereof. The method may be used for patients taking antidepressants such as tricyclic anti-depressants, monamine oxidase inhibitors, or selective serotonin reuptake inhibitors.

DOCUMENT TYPE:

Patent

LANGUAGE:

Chinese

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
CN 1375292	Α	20021023	CN 2002-111252	2002040.1
PRIORITY APPLN. INFO.:			CN 2002-111252	20020401
	0000			

ED Entered STN: 25 Aug 2003

AB The nasal preparation (such as nasal drop, spray, gel, ointment, membrane, powder, etc) for treating Parkinson's syndrome, male erection dysfunction, and female sexual function disorder consists of apomorphine or its medical salt, the antiemetic agent— containing nasal preparation, and adjuvant (such as diluter, antiseptic, stabilizer, penetration promoter, solubilizer, emulsifier, thickener, perfume, pH buffer, etc). The antiemetic agent is granisetron, ondansetron, domperidone, maxolon, nicotine, lobeline sulfate, buclizine HCl, cyclizine HCl, dimenhydrinate, scopolamine, chlorpromazine, prochlorperazine, thiethylperazine, oxypendyl HCl, benzamide, metopimazine, trimethobenzamide, benzquinamide HCl, diphenidol, menthol, mint oil, borneol, etc.

L42 ANSWER 8 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2003:300618 CAPLUS

DOCUMENT NUMBER:

138:309307

TITLE:

Apomorphine-containing dosage form for ameliorating

male erectile dysfunction

INVENTOR(S):

El-Rashidy, Ragab; Ronsen, Bruce

PATENT ASSIGNEE(S):

USA

SOURCE:

U.S. Pat. Appl. Publ., 36 pp., Cont.-in-part of U.S.

6,306,437. CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 7

PA	TENT :	NO.			KIN		DATE								D	ATE	
	2003 6566	: 0737: 368	15		A 1		2003	0417 0520			001-				2	0011	023
EP	9782	82			A2		2000	0209		EP 1	999-	1216	84		1	9950	421
EP	9782								a n	a n							
	R:			CH,	DE,	DK,	ES,	FR,	GB,	GR,	IT,	ыL,	LU,	ΝL,	SE,	PT,	IE,
***	C 7 7 0	SI,			~		1000				005				_		
	5770	606			A		1998 2000	0623		US I	995-	5464	98		1	9951	020
	6121	276			A		2000	0919		US 1	998~	1024	06		1	9980	622
	6306																
WO	2003																
	W:						AU,										
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	ΚP,	KR,	KZ,	LC,	LK,	LR,
							MD,										
							SE,										
							ZA,			•	•	•	•		•	·	•
	RW:	GH,	GM,	KE,	LS,	MW.	MZ,	SD,	SL,	SZ.	TZ.	UG,	ZM.	ZW.	AM.	AZ.	BY.
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							IT,										
							GQ,								,	20,	01,
EP	1448														2	0021	N 2 1
							ES,										
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examined for measurement of IC50. The most potent inhibitor observed was the selective estrogen receptor modulator, raloxifene (IC50 = 2.9 nM), and tamoxifen, estradiol, and ethinyl estradiol were also potent inhibitors. Other classes of drugs that demonstrated inhibition of aldehyde oxidase included phenothiazines, tricyclic antidepressants, tricyclic atypical antipsychotic agents, and dihydropyridine calcium channel blockers, along with some other drugs, including loratadine, cyclobenzaprine, amodiaquine, maprotiline, ondansetron, propafenone, domperidone, quinacrine, ketoconazole, verapamil, tacrine, and salmeterol. These findings are discussed in context to potential drug interactions that could be observed between these agents and drugs for which aldehyde oxidase is involved in metabolism and warrant investigation of the possibility of clin. drug interactions mediated by inhibition of this enzyme.

REFERENCE COUNT:

29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 6 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

PATENT ASSIGNEE(S):

2003:777120 CAPLUS

DOCUMENT NUMBER:

139:265812

TITLE:

Process for the preparation of rapidly disintegrating

tablet

INVENTOR(S):

Lee, Chang-Hyun; Woo, Jong-Soo; Chang, Hee-Chul

Hanmi Pharm. Co., Ltd., S. Korea

SOURCE:

U.S. Pat. Appl. Publ., 8 pp., Cont.-in-part of U.S.

Pat. Appl. 2002 1,617.

CODEN: USXXCO

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	ENT NO.	KIND	DATE	API	PLICATION NO.		DATE
						-	
US	2003185886	A1	20031002	US	2003-391103		20030317
US	2002001617	A1	20020103	US	2001-865264		20010525
PRIORITY	APPLN. INFO.:			KR	2000-28667	Α	20000526
				US	2001-865264	A2	20010525

ED Entered STN: 03 Oct 2003

AB The present invention relates to a process for the preparation of a tablet having an enhanced strength as well as a high disintegrating rate in the oral cavity, which comprises: spray-drying an active ingredient to obtain a spray-dried particulate containing the active ingredient; mixing the spray-dried particulate, a sublimable substance suitable for oral administration, a poly(ethylene glycol), and a pharmaceutically acceptable additive; tableting the mixture; and drying the resulting tablet to sublime the sublimable substance until the tablet becomes porous. For example, ondansetron was dissolved in methanol and the solution was subjected to spray drying to obtain a particulate material, then the particulate was mixed with menthol, mannitol, xylitol, polyethylene glycol, stevioside, PVP, Mg stearate, and silica. The resulting mixture was tableted and dried at 45° for 24 h to sublime menthol to obtain a rapidly disintegrating tablet.

L42 ANSWER 7 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 20

2003:660391 CAPLUS

DOCUMENT NUMBER:

139:219303

TITLE:

Compound nasal preparation for alleviating the side

effect of apomorphine

INVENTOR(S):

Chen, Guoshen; Jiang, Xinguo; Zhang, Wanggang; Lu,

Wei; Zheng, Gaoli; Chen, Jun

PATENT ASSIGNEE(S):

Zhejiang Academy of Medical Sciences, Peop. Rep.

China; Fudan Univ.

SOURCE:

Faming Zhuanli Shenqing Gongkai Shuomingshu, 9 pp.

CODEN: CNXXEV

scopolamine.

L42 ANSWER 4 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

2004:220186 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 140:276172

TITLE: Taste masked dosage forms comprising acrylic polymers

and processes for their preparation

Murpani, Deepak; Arora, Vinod Kumar; Malik, Rajiv INVENTOR(S):

Ranbaxy Laboratories Limited, India PATENT ASSIGNEE(S):

PCT Int. Appl., 23 pp. SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	ENT NO.			KIND DATE			APPLICATION NO.						DATE				
WO	2004022037				A1 20040318			WO 2003-IB3779						20030904			
	W:	ΑE,	AG,	AL,	AM,	AT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BY,	ΒZ,	CA,	CH,	CN,
		CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	ES,	FI,	GB,	GD,	GE,	GH,
		GM,	HR,	ΗU,	ID,	IL,	IN,	IS,	JP,	KE,	KG,	KP,	KR,	ΚZ,	LC,	LK,	LR,
		LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	ΜZ,	NI,	NO,	ΝZ,	OM,
		PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,	ТJ,	TM,	TN,
		TR,	TT,	ΤŻ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	zw			
	RW:	GH,	GM,	KE,	LS,	MW,	ΜZ,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,	ΑZ,	BY,
		KG,	ΚZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,	EE,	ES,
		FI,	FR,	GB,	GR,	HU,	ΙE,	IT,	LU,	MC,	NL,	PT,	RO,	SE,	SI,	SK,	TR,
		BF,	ВJ,	CF,	CG,	CI,	CM,	GA,	GN,	GQ,	GW,	ML,	MR,	ΝE,	SN,	TD,	TG
PRIORITY	APP	LN.	INFO	. : ·						IN 2	002-	DE 90	3	1	A 20	0020	904

ED Entered STN: 19 Mar 2004

The invention relates to taste masked dosage forms utilizing low amts. of AΒ taste masking polymer, and simple and economical processes for the preparation of the taste masked dosage forms. The taste-masked dosage form includes one or more drugs and one or more cationic polymers synthesized from dimethylaminoethyl methacrylate and neutral methacrylic acid esters. $\operatorname{wt/wt}$ ratio of the drug to polymer is less than about one to two. Hard gelatin capsules contained topiramate 15, Eudragit EPO 26, Et cellulose (low viscosity) 3.7, titanium dioxide 1.0, nonpareil seeds 45.3, talc 8.9, iso-Pr alc./water (3:1) q.s. 100%.

THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 6 RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L42 ANSWER 5 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

2004:56700 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER:

141:150902

TITLE: Human liver aldehyde oxidase: inhibition by 239 drugs Obach, R. Scott; Huynh, Phuong; Allen, Mary C.; AUTHOR (S):

Beedham, Christine

Groton Laboratories, Pfizer Global Research and CORPORATE SOURCE:

Development, Groton, CT, USA

Journal of Clinical Pharmacology (2004), 44(1), 7-19 SOURCE:

CODEN: JCPCBR; ISSN: 0091-2700

PUBLISHER: Sage Publications

DOCUMENT TYPE: Journal English LANGUAGE: Entered STN: 23 Jan 2004 ED

AB The authors tested 239 frequently used drugs and other compds. for their potential to inhibit the drug-metabolizing enzyme, aldehyde oxidase, in human liver cytosol. A sensitive, moderate throughput HPLC-MS assay was developed for 1-phthalazinone, the aldehyde oxidase-catalyzed product of phthalazine oxidation Inhibition of this activity was examined for the 239 drugs and other compds. of interest at a test concentration of 50 μM . Thirty-six compds. exhibited greater than 80% inhibition and were further

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
KR 2002096440 PRIORITY APPLN. INFO.:	A 2004	20021231	KR 2001-34884 KR 2001-34884	20010620 20010620

Entered STN: 15 Nov 2004

A process of preparing an apomorphine formulation for oral use by granulation of apomorphine, spraying a coating liquid at low temperature and spraying the coating liquid at high speed while floating the coating liquid at low temperature is

provided. Whereby, the formulation is excellent in treatment of erectile dysfunction. An excipient, binder and solvent are added to a mixed powder containing 1 to 10% by weight of apomorphine or

acid

salts thereof, 20 to 40% by weight of ascorbic acid, 10 to 20% by weight of domperidone to produce apomorphine granules. A coating liquid comprising 1 to 30% by weight of a coating base, 0.1 to 1.0% by weight of a plasticizer and

а

solvent is coated on 30 to 40% by weight of the granules at 30 to 40 $^{\circ}$ to produce first coated granules. A coating liquid comprising 1 to 30% by weight of a coating base and 0.1 to 1.0% by weight of a plasticizer is coated

on

30 to 40% by weight of the first coated granules at 30 to 40° to produce second coated granules. Thereafter, 40 to 50% by weight of apomorphine, 20 to 30% by weight of the first coated granules and 30% by weight of the second coated granules are mixed.

L42 ANSWER 3 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2004:963818 CAPLUS

DOCUMENT NUMBER:

142:183405

TITLE:

SOURCE:

Formulation for nasal administration of apomorphine

and production thereof

INVENTOR(S):

Kim, Hui Jun; Park, Dong U.

PATENT ASSIGNEE(S):

Il-Yang Pharm. Co., Ltd., S. Korea Repub. Korean Kongkae Taeho Kongbo, No pp. given

CODEN: KRXXA7

DOCUMENT TYPE:

Patent

LANGUAGE:

Korean

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATIÒN NO.	DATE
KR 2003000397 PRIORITY APPLN. INFO.:	A	20030106	KR 2001-36157 KR 2001-36157	20010625 20010625

ED Entered STN: 12 Nov 2004

A process for preparing a formulation for nasal administration using AB apomorphine by dissolving apomorphine used as a composition for treating erectile impotence, together with an antiemetic, antioxidant, saccharides and pharmaceutically acceptable excipients, in a solvent and then drying is provided. Whereby, the formulation has an excellent therapeutic effect for treatment of erectile dysfunction while remarkably reducing adverse effects such as nausea, vertigo, etc. A mixture of 5 to 20 % by weight of apomorphine or acid addition salts thereof,

2.5

to 10 % by weight of an antiemetic, 2.5 % by weight of an antioxidant, 2.5 to

10 by

\$ by weight of an aqueous natural or synthetic polymer material and 30 to 75 \$

weight of sugar alcs. or disaccharides is dissolved in purified water and then dried in a spray drier at an inlet temperature of 100 to 150°C and an outlet temperature of 70 to 120°C. The antiemetic is selected from metoclopramide, chlorpromazine, domperidone, dimenhydrinate and

=> s 142 not 130 L43 6 S L30

L44 20 L42 NOT L43

=> d 142 1-20 ibib ed abs

L42 ANSWER 1 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:76270 CAPLUS

DOCUMENT NUMBER: 142:148827

TITLE: Phosphodiesterase 5 inhibitor-5-HTla agonist

combination for the treatment of sexual

dysfunction

INVENTOR(S): Naylor, Alasdair Mark; Van der Graaf, Pieter Hadewijn;

Wayman, Christopher Peter

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc. .

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE: LANGUAGE:

Patent English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

P	ATENT	NO.			KIN	D	DATE		7	APPL	ICAT	ION I	NO.		D.	ATE	
W	0 2005	0071	66		A1	_	2005	0127	1	WO 2	004-	IB22	- 86	-	2	0040	712
	W:						AU,										
		CN,	CO,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
							ID,										
		LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,
		NO,	NΖ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
		ТJ,	TM,	TN,	TR,	TT,	ΤZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW
	RW:	BW,	GH,	GM,	ΚE,	LS,	MW,	ΜZ,	NA,	SD,	SL,	SZ,	TZ,	UG,	ZM,	ZW,	AM,
		ΑZ,	BY,	KG,	ΚZ,	MD,	RU,	ТJ,	TM,	AT,	BE,	BG,	CH,	CY,	CZ,	DE,	DK,
		EE,	ES,	FI,	FR,	GB,	GR,	HU,	IE,	IT,	LU,	MC,	NL,	PL,	PT,	RO,	SE,
		SI,	SK,	TR,	BF,	ВJ,	CF,	CG,	CI,	CM,	GΑ,	GN,	GQ,	GW,	ML,	MR,	NE,
		SN,	TD,	TG									•				
U	S 2005	0651	58		A 1		2005	0324	1	US 2	004-	8836:	22		2	0040	701
PRIORI	TY APP	LN.	INFO	. :				2	(GB 2	003-	1667	3	i	A 2	0030	716
									(GB 2	003-	1809	5	i	A 2	0030	801
									(GB 2	003-	2130	В	1	A 2	0030	911
									1	US 2	003-	5120	30P		P 2	0031	017
									1	US 2	003-	5131	25P	1	P 2	0031	021

ED Entered STN: 28 Jan 2005

The invention discloses the use of cyclic guanosine 3', 5'-monophosphate AB phosphodiesterase type 5 (PDE5) inhibitors in combination with 5-HTla agonists for the treatment of sexual dysfunction, particularly female sexual arousal

disorder (FSAD) with concomitant hypoactive sexual desire disorder (HSDD).

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

7

L42 ANSWER 2 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

REFERENCE COUNT:

2004:970205 CAPLUS

DOCUMENT NUMBER:

142:183408

TITLE:

Controlled release oral apomorphine formulation and

THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS

production thereof

INVENTOR(S):

Kim, Su Gyun; Park, Dong U.

PATENT ASSIGNEE(S):

Il-Yang Pharm. Co., Ltd., S. Korea

SOURCE:

Repub. Korean Kongkae Taeho Kongbo, No pp. given

CODEN: KRXXA7

DOCUMENT TYPE:

Patent

LANGUAGE:

Korean

FAMILY ACC. NUM. COUNT:

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L11 (
L12 (
         4907) SEA FILE=REGISTRY SSS FUL L1
L13 (
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L14 (
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L15 (
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L16 (
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L17 (
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L18
          63399 S (SEXUAL DYSFUNCTION? OR SEXUAL DISFUNCTION? OR ERECTILE DYSFU
L19
          1658 S (FEMALE SEXUAL DYSFUNCTION? OR FEMALE SEXUAL DISFUNCTION? OR
L20
          1081 S BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO"
L21
L22
          63430 S L19 OR L20
      343217 S CLITOR? OR GENITAL? OR SEXUAL GENITAL? OR PENIS? OR PENILE? O
L23
         381006 S L22 OR L23
L24
             10 S L24 AND (L18 OR L21)
L25
              6 DUP REM L25 (4 DUPLICATES REMOVED)
L26
L27
           3431 S ((INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?)) OR
           4411 S L18 OR L21 OR L27
L28
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L29
L30
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            141 S (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANNEL
L31
            609 S BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO"
L32
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L33
L34
           2210 S L31 OR L32 OR L33
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L35
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L36
     FILE 'CAPLUS' ENTERED AT 12:32:08 ON 14 APR 2005
           6484 S L36
L37
            194 S L34 AND L37
L38
              0 S L38 AND (L19 OR L20 OR L23)
L39
L40
              0 S L38 AND (SEX? DYSF?)
              2 S L38 AND (SEXUAL DYSFUNCTION? OR PENIS? OR PENILE? OR ERECTILE
L41
=> d cost
COST IN U.S. DOLLARS
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                                                                TOTAL
                                                      ENTRY
                                                               SESSION
                                                                 46.11
CONNECT CHARGES
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NETWORK CHARGES
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FULL ESTIMATED COST
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CA SUBSCRIBER PRICE
IN FILE 'CAPLUS' AT 12:35:14 ON 14 APR 2005
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ACCESSION NUMBER:
                         2001:905334 CAPLUS
DOCUMENT NUMBER:
                         136:241373
TITLE:
                         Activation of endothelial cell IKCa with
                         1-ethy1-2-
                         benzimidazolinone evokes smooth
                         muscle hyperpolarization in rat isolated
                        mesenteric artery
AUTHOR(S):
                         Walker, S. D.; Dora, K. A.; Ings, N. T.; Crane, G. J.;
                         Garland, C. J.
                         Department of Pharmacy and Pharmacology, University of
CORPORATE SOURCE:
                         Bath, Bath, BA2 7AY, UK
                         British Journal of Pharmacology (2001), 134(7),
SOURCE:
                         1548-1554
                         CODEN: BJPCBM; ISSN: 0007-1188
PUBLISHER:
                         Nature Publishing Group
DOCUMENT TYPE:
                         Journal
LANGUAGE:
                         English
     Entered STN: 16 Dec 2001
     1 In rat small mesenteric arteries contracted with phenylephrine,
AB
     1-ethyl-2-benzimidazolinone (
     1-EBIO; 3-300 \muM) evoked concentration-dependent relaxation
     that, above 100 µM, was associated with smooth muscle
     hyperpolarization. 2 1-EBIO-evoked hyperpolarization
     (maximum 22.1\pm3.6 mV with 300 \muM, n = 4) was endothelium-dependent and
     inhibited by charybdotoxin (ChTX 100 nM; n = 4) but not iberiotoxin (IbTX
     100 nM; n = 4). 3 In endothelium-intact arteries, smooth
     muscle relaxation to 1-EBIO was not altered by
     either of the potassium channel blockers ChTX (100 nM; n = 7), or IbTX
     (100 nM; n = 4), or raised extracellular K+ (25 mM). Removal of the
     endothelium shifted the relaxation curve to the right but did not reduce
     the maximum relaxation. 4 In freshly isolated mesenteric endothelial cells,
     1-EBIO (600 \mu\text{M}) evoked a ChTX-sensitive outward
     K-current. In contrast, 1-EBIO had no effect on
     smooth muscle cell conductance whereas NS 1619 (33
     \mu M) stimulated an outward current while having no effect on the
     endothelial cells. 5 These data show that with concns. greater than 100
     μM, 1-EBIO selectively activates outward current in
     endothelial cells, which presumably underlies the smooth
     muscle hyperpolarization and a component of the relaxation.
     Sensitivity to block with charybdotoxin but not iberiotoxin indicates this
     current is due to activation of IKCa. However, 1-
     EBIO can also relax the smooth muscle by an
     undefined mechanism, independent of any change in membrane potential.
REFERENCE COUNT:
                         28
                               THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT
=> d his
     (FILE 'HOME' ENTERED AT 12:07:55 ON 14 APR 2005)
     FILE 'CAPLUS' ENTERED AT 12:08:10 ON 14 APR 2005
               ACTIVATE L09939093/L
L1
                STR
L2
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L3
              0) SEA FILE=REGISTRY EXA FUL L1
L4
           4907) SEA FILE=REGISTRY SSS FUL L1
L5
             61) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                L2
L6
            112) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                L2 OR "1-ETHYL-2-BENZIMIDAZOLIN
L7
              1) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                L6 AND (SEXUAL DYSFUNCTION? OR
                                                L6 AND GENITALIA?
L8
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L9
              1) SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (SEXUAL?)
L10
                STR
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30354 CORPUS (CORPUS OR CORPUSES OR CORPORA) 1082 CAVERNOS? 887 CORPUS CAVERNOS? (CORPUS (W) CAVERNOS?) 156326 SMOOTH 339 SMOOTHS 156628 SMOOTH (SMOOTH OR SMOOTHS) 311391 MUSCLE? 65892 SMOOTH MUSCLE? (SMOOTH(W)MUSCLE?) 2 L38 AND (SEXUAL DYSFUNCTION? OR PENIS? OR PENILE? OR ERECTILE? L41 OR CLITOR? OR ERECTION? OR IMPOTEN? OR TUMESCEN? OR CORPUS CAVER NOS? OR SMOOTH MUSCLE?) => d 141 1-2 ibib ed abs L41 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN ACCESSION NUMBER: 2002:262156 CAPLUS DOCUMENT NUMBER: 137:890 TITLE: Characterization of an apamin-sensitive small-conductance Ca2+-activated K+ channel in porcine coronary artery endothelium: relevance to EDHF AUTHOR(S): Burnham, M. P.; Bychkov, R.; Feletou, M.; Richards, G. R.; Vanhoutte, P. M.; Weston, A. H.; Edwards, G. CORPORATE SOURCE: School of Biological Sciences, University of Manchester, Manchester, M13 9PT, UK British Journal of Pharmacology (2002), 135(5), SOURCE: 1133-1143 CODEN: BJPCBM; ISSN: 0007-1188 PUBLISHER: Nature Publishing Group DOCUMENT TYPE: Journal LANGUAGE: English ED Entered STN: 09 Apr 2002 AB The apamin-sensitive small-conductance Ca2+-activated K+ channel (SKCa) was characterized in porcine coronary arteries. In intact arteries, 100 nM substance P and 600 μM 1-ethyl-2benzimidazolinone (1-EBIO) produced endothelial cell hyperpolarizations (27.8 mV and 24.1 mV, resp.). Charybdotoxin (100 nM) abolished the 1-EBIO response but substance P continued to induce a hyperpolarization (25.8 mV). In freshly-isolated endothelial cells, outside-out patch recordings revealed a unitary K+ conductance of 6.8 pS. The open-probability was increased by Ca2+ and reduced by apamin (100 nM). Substance P activated an outward current under whole-cell perforated-patch conditions and a component of this current (38%) was inhibited by apamin. A second conductance of 2.7 pS inhibited by d-tubocurarine was observed infrequently. The mRNA encoding the SK2 and SK3, but not the SK1, subunits of SKCa was detected by RT-PCR in samples of endothelium. Western blotting indicated that SK3 protein was abundant in samples of endothelium compared to whole arteries. SK2 protein was present in whole artery nuclear fractions. Immunofluorescent labeling confirmed that SK3 was highly expressed at the plasmalemma of endothelial cells and was not expressed in smooth muscle SK2 was restricted to the perinuclear regions of both endothelial and smooth muscle cells. In conclusion, the porcine coronary artery endothelium expresses an apamin-sensitive SKCa containing the SK3 subunit. These channels are likely to confer all or part of the

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

apamin-sensitive component of the endothelium-derived hyperpolarizing

factor (EDHF) response.

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L19
           1658 S (FEMALE SEXUAL DYSFUNCTION? OR FEMALE SEXUAL DISFUNCTION? OR
L20
           1081 S BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO"
L21
L22
          63430 S L19 OR L20
         343217 S CLITOR? OR GENITAL? OR SEXUAL GENITAL? OR PENIS? OR PENILE? O
L23
L24
         381006 S L22 OR L23
             10 S L24 AND (L18 OR L21)
L25
L26
              6 DUP REM L25 (4 DUPLICATES REMOVED)
L27
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L29
             32 S L24 AND L28
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L30
     FILE 'STNGUIDE' ENTERED AT 12:22:03 ON 14 APR 2005
     FILE 'CAPLUS' ENTERED AT 12:28:09 ON 14 APR 2005
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L31
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L32
L33
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L35
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L36
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L37
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           194 L34 AND L37
=> s 138 and (119 or 120 or 123)
L39
             0 L38 AND (L19 OR L20 OR L23)
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         45363 DYSF?
          1031 SEX? DYSF?
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L40
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erection? or impoten? or tumescen? or corpus cavernos? or smooth muscle?)
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         29940 SEXUAL
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          2881 PENIS?
          1933 PENILE?
          2045 ERECTILE?
           503 CLITOR?
          2361 ERECTION?
          2597 IMPOTEN?
           204 TUMESCEN?
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          7353 CORPORA
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L36 13897 SEA SSS FUL L35

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ENTRY SESSION
FULL ESTIMATED COST
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448.28

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE

CA SUBSCRIBER PRICE SESSION 0.00 -5.84

TOTAL

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FILE COVERS 1907 - 14 Apr 2005 VOL 142 ISS 16 FILE LAST UPDATED: 13 Apr 2005 (20050413/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> s 136 L37 6484 L36

=> d his

(FILE 'HOME' ENTERED AT 12:07:55 ON 14 APR 2005)

FILE 'CAPLUS' ENTERED AT 12:08:10 ON 14 APR 2005 ACTIVATE L09939093/L

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L3	(0)SEA	FILE=REGISTRY EXA FUL L1	
L4	(4907) SEA	FILE=REGISTRY SSS FUL L1	ir I
L5	(61) SEA	FILE=CAPLUS ABB=ON PLU=ON	L2
L6	(112) SEA	FILE=CAPLUS ABB=ON PLU=ON	L2 OR "1-ETHYL-2-BENZIMIDAZOLIN
L7	(1)SEA	FILE=CAPLUS ABB=ON PLU=ON	L6 AND (SEXUAL DYSFUNCTION? OR
rs	(0)SEA	FILE=CAPLUS ABB=ON PLU=ON	L6 AND GENITALIA?
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L11	(50) SEA	FILE=REGISTRY SSS SAM L10	
L12	(4907) SEA	FILE=REGISTRY SSS FUL L1	
L13	(13889) SEA	FILE=REGISTRY SSS FUL L10	
L14	(58) SEA	FILE=CAPLUS ABB=ON PLU=ON	L13 AND (SEXUAL DYSFUNCTION? OR
L15	(1)SEA	FILE=CAPLUS ABB=ON PLU=ON	L14 AND (CALCIUM CHANNEL?)
L16	(5)SEA	FILE=CAPLUS ABB=ON PLU=ON	L14 AND CALCIUM?
L17	(53) SEA	FILE=CAPLUS ABB=ON PLU=ON	L14 NOT (L15 OR L16)

=> s 131 or 132 or 133 L34 2210 L31 OR L32 OR L33

=> s 113 and 134

SUBSTANCE QUERIES NOT VALID IN THIS FILE

The logic expression entered contains L#s or saved query names which correspond to structures built by the STRUCTURE command or to screen sets. These must be searched in a substance file such as the REGISTRY file. In some files you may use a Registry Number answer set from a structure search as a search term or profile in some bibliographic file containing Registry Numbers, e.g. the CA file. For an explanation, enter "HELP CROSSOVER" at an arrow prompt (=>).

=> file registry COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION FULL ESTIMATED COST 59.40 286.95 DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION CA SUBSCRIBER PRICE 0.00 -5.84

FILE 'REGISTRY' ENTERED AT 12:31:39 ON 14 APR 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 American Chemical Society (ACS)

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STRUCTURE FILE UPDATES: 13 APR 2005 HIGHEST RN 848462-79-3 DICTIONARY FILE UPDATES: 13 APR 2005 HIGHEST RN 848462-79-3

TSCA INFORMATION NOW CURRENT THROUGH JANUARY 18, 2005

Please note that search-term pricing does apply when conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Experimental and calculated property data are now available. For more information enter HELP PROP at an arrow prompt in the file or refer to the file summary sheet on the web at: http://www.cas.org/ONLINE/DBSS/registryss.html

Uploading C:\Program Files\Stnexp\Queries\09939093a.str

L35 STRUCTURE UPLOADED

=> s 135 full FULL SEARCH INITIATED 12:32:02 FILE 'REGISTRY' FULL SCREEN SEARCH COMPLETED - 82442 TO ITERATE

100.0% PROCESSED 82442 ITERATIONS

```
("IK" OR "IKS")
        195209 "CA2+"
                 ("CA2")
        735624 "CA"
         11539 "CAS"
        745351 "CA"
                 ("CA" OR "CAS")
       8348452 "2"
          5160 "CA(2+)"
                  ("CA"(W)"2")
           395 ((INTERMEDIATE CONDUCTANCE) OR "IK") (5A) ("CA2+" OR "CA(2+)")
L33
          1637 ((INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?)) OR
               ((INTERMEDIATE CONDUCTANCE) (5A) "CA2+") OR "IKCA" OR "KCA" OR
               (((INTERMEDIATE CONDUCTANCE) OR "IK") (5A) ("CA2+" OR "CA(2+)"))
=> d his
     (FILE 'HOME' ENTERED AT 12:07:55 ON 14 APR 2005)
     FILE 'CAPLUS' ENTERED AT 12:08:10 ON 14 APR 2005
                ACTIVATE L09939093/L
L1
                STR
L2
             50) SEA FILE=REGISTRY SSS SAM L1
L3
              0) SEA FILE=REGISTRY EXA FUL L1
L4
           4907) SEA FILE=REGISTRY SSS FUL L1
L5
             61) SEA FILE=CAPLUS ABB=ON PLU=ON L2
L6
            112) SEA FILE=CAPLUS ABB=ON PLU=ON L2 OR "1-ETHYL-2-BENZIMIDAZOLIN
L7
              1) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                L6 AND (SEXUAL DYSFUNCTION? OR
rs
              0) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                L6 AND GENITALIA?
              1) SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (SEXUAL?)
L9
L10
                STR
L11 (
             50) SEA FILE=REGISTRY SSS SAM L10
L12 (
           4907) SEA FILE=REGISTRY SSS FUL L1
L13 (
          13889) SEA FILE=REGISTRY SSS FUL L10
L14 (
             58) SEA FILE=CAPLUS ABB=ON PLU=ON L13 AND (SEXUAL DYSFUNCTION? OR
L15 (
              1) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                                L14 AND (CALCIUM CHANNEL?)
L16 (
              5) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON L14 AND CALCIUM?
L17 (
             53) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON L14 NOT (L15 OR L16)
     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 12:08:44 ON 14
     APR 2005
            487 S (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANNEL
L18
L19
          63399 S (SEXUAL DYSFUNCTION? OR SEXUAL DISFUNCTION? OR ERECTILE DYSFU
           1658 S (FEMALE SEXUAL DYSFUNCTION? OR FEMALE SEXUAL DISFUNCTION? OR
L20
L21
           1081 S BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO"
L22
          63430 S L19 OR L20
         343217 S CLITOR? OR GENITAL? OR SEXUAL GENITAL? OR PENIS? OR PENILE? O
L23
L24
         381006 S L22 OR L23
L25
             10 S L24 AND (L18 OR L21)
L26
              6 DUP REM L25 (4 DUPLICATES REMOVED)
L27
           3431 S ((INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?)) OR
           4411 S L18 OR L21 OR L27
L28
             32 S L24 AND L28
L29
             20 DUP REM L29 (12 DUPLICATES REMOVED)
L30
     FILE 'STNGUIDE' ENTERED AT 12:22:03 ON 14 APR 2005
     FILE 'CAPLUS' ENTERED AT 12:28:09 ON 14 APR 2005
            141 S (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANNEL
L31
L32
            609 S BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO"
L33
           1637 S ((INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?)) OR
```

```
62 "EBIO"
            34 "EBIOS"
            96 "EBIO"
                 ("EBIO" OR "EBIOS")
       8234744 "1"
            62 "EBIO"
            34 "EBIOS"
            96 "EBIO"
                 ("EBIO" OR "EBIOS")
               "1-EBIO"
            48
                 ("1"(W) "EBIO")
L32
           609 BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO"
               OR "1-EBIO"
=> s ((intermediate conductance) (5A) (calcium? or potassium?)) or ((intermediate
conductance) (5A) "Ca2+") or "IKCa" or "KCa" or (((intermediate conductance) or
"IK") (5A) ("Ca2+" or "Ca(2+)"))
        448272 INTERMEDIATE
        140537 INTERMEDIATES
        546226 INTERMEDIATE
                  (INTERMEDIATE OR INTERMEDIATES)
         63127 CONDUCTANCE
          6780 CONDUCTANCES
         66056 CONDUCTANCE
                  (CONDUCTANCE OR CONDUCTANCES)
           237 INTERMEDIATE CONDUCTANCE
                 (INTERMEDIATE (W) CONDUCTANCE)
        717995 CALCIUM?
        556631 POTASSIUM?
            91 (INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?)
        448272 INTERMEDIATE
        140537 INTERMEDIATES
        546226 INTERMEDIATE
                  (INTERMEDIATE OR INTERMEDIATES)
         63127 CONDUCTANCE
          6780 CONDUCTANCES
         66056 CONDUCTANCE
                  (CONDUCTANCE OR CONDUCTANCES)
           237 INTERMEDIATE CONDUCTANCE
                 (INTERMEDIATE (W) CONDUCTANCE)
        195209 "CA2+"
                 ("CA2")
            99 (INTERMEDIATE CONDUCTANCE) (5A) "CA2+"
           109 "IKCA"
             1 "IKCAS"
           109 "IKCA"
                 ("IKCA" OR "IKCAS")
          1148 "KCA"
            10 "KCAS"
          1153 "KCA"
                ("KCA" OR "KCAS")
        448272 INTERMEDIATE
        140537 INTERMEDIATES
        546226 INTERMEDIATE
                  (INTERMEDIATE OR INTERMEDIATES)
         63127 CONDUCTANCE
          6780 CONDUCTANCES
         66056 CONDUCTANCE
                  (CONDUCTANCE OR CONDUCTANCES)
           237 INTERMEDIATE CONDUCTANCE
                 (INTERMEDIATE (W) CONDUCTANCE)
          3378 "IK"
           797 "IKS"
          4057 "IK"
```

```
L4
           4907) SEA FILE=REGISTRY SSS FUL L1
L5
             61) SEA FILE=CAPLUS ABB=ON PLU=ON L2
L6
            112) SEA FILE=CAPLUS ABB=ON
                                         PLU=ON L2 OR "1-ETHYL-2-BENZIMIDAZOLIN
L7
              1) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON L6 AND (SEXUAL DYSFUNCTION? OR
rs
              O) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                L6 AND GENITALIA?
              1) SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (SEXUAL?)
L9
L10
                STR
L11 (
             50) SEA FILE=REGISTRY SSS SAM L10
L12 (
           4907) SEA FILE=REGISTRY SSS FUL L1
L13 (
          13889) SEA FILE=REGISTRY SSS FUL L10
L14 (
             58) SEA FILE=CAPLUS ABB=ON PLU=ON L13 AND (SEXUAL DYSFUNCTION? OR
L15 (
              1) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON L14 AND (CALCIUM CHANNEL?)
L16 (
              5) SEA FILE=CAPLUS ABB=ON PLU=ON L14 AND CALCIUM?
             53) SEA FILE=CAPLUS ABB=ON PLU=ON L14 NOT (L15 OR L16)
L17 (
=> s (intermediate conductance calcium activated potassium channel?) or "IKCa"
        448272 INTERMEDIATE
        140537 INTERMEDIATES
        546226 INTERMEDIATE
                  (INTERMEDIATE OR INTERMEDIATES)
         63127 CONDUCTANCE
          6780 CONDUCTANCES
         66056 CONDUCTANCE
                  (CONDUCTANCE OR CONDUCTANCES)
        717357 CALCIUM
            32 CALCIUMS
        717360 CALCIUM
                  (CALCIUM OR CALCIUMS)
        459100 ACTIVATED
        556453 POTASSIUM
            15 POTASSIUMS
        556455 POTASSIUM
                  (POTASSIUM OR POTASSIUMS)
        322740 CHANNEL?
            40 INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANNEL?
                 (INTERMEDIATE(W)CONDUCTANCE(W)CALCIUM(W)ACTIVATED(W)POTASSIUM(
                 W) CHANNEL?)
           109 "IKCA"
             1 "IKCAS"
           109 "IKCA"
                  ("IKCA" OR "IKCAS")
L31
           141 (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANNEL?)
               OR "IKCA"
=> s benzimidazolinone? or "1-ethyl-2-benzimidazolinone" or "EBIO" or "1-EBIO"
           550 BENZIMIDAZOLINONE?
       8234744 "1"
        426100 "ETHYL"
            24 "ETHYLS"
        426119 "ETHYL"
                 ("ETHYL" OR "ETHYLS")
        607999 "ET"
          6920 "ETS"
        613429 "ET"
                  ("ET" OR "ETS")
        910986 "ETHYL"
                 ("ETHYL" OR "ET")
       8348452 "2"
           525 "BENZIMIDAZOLINONE"
           103 "BENZIMIDAZOLINONES"
           549 "BENZIMIDAZOLINONE"
                 ("BENZIMIDAZOLINONE" OR "BENZIMIDAZOLINONES")
            51 "1-ETHYL-2-BENZIMIDAZOLINONE"
                  ("1"(W)"ETHYL"(W)"2"(W)"BENZIMIDAZOLINONE")
```

ENTRY SESSION 0.00 -5.84

CA SUBSCRIBER PRICE

IN FILE 'STNGUIDE' AT 12:27:50 ON 14 APR 2005

=> file caplus

COST IN U.S. DOLLARS SINCE FILE TOTAL ENTRY SESSION

FULL ESTIMATED COST 0.60 227.55

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL ENTRY SESSION

CA SUBSCRIBER PRICE 0.00 -5.84

FILE 'CAPLUS' ENTERED AT 12:28:09 ON 14 APR 2005 USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT. PLEASE SEE "HELP USAGETERMS" FOR DETAILS. COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY (ACS)

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FILE COVERS 1907 - 14 Apr 2005 VOL 142 ISS 16 FILE LAST UPDATED: 13 Apr 2005 (20050413/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

=> d his 1-17 1-17 NOT VALID FOR HISTORY RANGE You may enter one of the following:

- 1. L1- to display your entire session history
- 2. A specific L-number or range of L-numbers to be displayed
- 3. L# to display the most recently created L-number
- 4. A number, N, to display the N most recent L-numbers ENTER (L1-), L#, OR ?:11-17 L1-17 NOT VALID FOR HISTORY RANGE

You may enter one of the following:

- 1. L1- to display your entire session history
- 2. A specific L-number or range of L-numbers to be displayed
- 3. L# to display the most recently created L-number
- 4. A number, N, to display the N most recent L-numbers ENTER (L1-), L#, OR ?:11-117

(FILE 'HOME' ENTERED AT 12:07:55 ON 14 APR 2005)

FILE 'CAPLUS' ENTERED AT 12:08:10 ON 14 APR 2005 ACTIVATE L09939093/L

L1 STR
L2 (50)SEA FILE=REGISTRY SSS SAM L1
L3 (0)SEA FILE=REGISTRY EXA FUL L1

FILE 'STNGUIDE' ENTERED AT 12:22:03 ON 14 APR 2005
USE IS SUBJECT TO THE TERMS OF YOUR CUSTOMER AGREEMENT
COPYRIGHT (C) 2005 AMERICAN CHEMICAL SOCIETY, JAPAN SCIENCE
AND TECHNOLOGY CORPORATION, AND FACHINFORMATIONSZENTRUM KARLSRUHE

FILE CONTAINS CURRENT INFORMATION.
LAST RELOADED: Apr 8, 2005 (20050408/UP).

=> d his

FULL ESTIMATED COST

DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

(FILE 'HOME' ENTERED AT 12:07:55 ON 14 APR 2005)

FILE 'CAPLUS' ENTERED AT 12:08:10 ON 14 APR 2005 ACTIVATE L09939093/L

```
ACTIVATE L09939093/L
L1
                STR
L2
             50) SEA FILE=REGISTRY SSS SAM L1
    (
L3
              0) SEA FILE=REGISTRY EXA FUL L1
           4907) SEA FILE=REGISTRY SSS FUL L1
L4
L5
            61) SEA FILE=CAPLUS ABB=ON PLU=ON L2
L6
            112) SEA FILE=CAPLUS ABB=ON PLU=ON L2 OR "1-ETHYL-2-BENZIMIDAZOLIN
L7
            1) SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (SEXUAL DYSFUNCTION? OR
L8
              0) SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND GENITALIA?
L9
              1) SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (SEXUAL?)
L10
                STR
L11 (
             50)SEA FILE=REGISTRY SSS SAM L10
L12 (
          4907) SEA FILE=REGISTRY SSS FUL L1
L13 (
          13889) SEA FILE=REGISTRY SSS FUL L10
L14 (
             58) SEA FILE=CAPLUS ABB=ON PLU=ON L13 AND (SEXUAL DYSFUNCTION? OR
L15 (
              1) SEA FILE=CAPLUS ABB=ON PLU=ON L14 AND (CALCIUM CHANNEL?)
L16 (
              5) SEA FILE=CAPLUS ABB=ON PLU=ON L14 AND CALCIUM?
             53) SEA FILE=CAPLUS ABB=ON PLU=ON L14 NOT (L15 OR L16)
L17 (
     FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 12:08:44 ON 14
     APR 2005
            487 S (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANNEL
L18
L19
          63399 S (SEXUAL DYSFUNCTION? OR SEXUAL DISFUNCTION? OR ERECTILE DYSFU
L20
          1658 S (FEMALE SEXUAL DYSFUNCTION? OR FEMALE SEXUAL DISFUNCTION? OR
L21
           1081 S BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO"
L22
          63430 S L19 OR L20
L23
         343217 S CLITOR? OR GENITAL? OR SEXUAL GENITAL? OR PENIS? OR PENILE? O
         381006 S L22 OR L23
L24
L25
             10 S L24 AND (L18 OR L21)
L26
              6 DUP REM L25 (4 DUPLICATES REMOVED)
L27
           3431 S ((INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?)) OR
           4411 S L18 OR L21 OR L27
L28
L29
             32 S L24 AND L28
L30
             20 DUP REM L29 (12 DUPLICATES REMOVED)
     FILE 'STNGUIDE' ENTERED AT 12:22:03 ON 14 APR 2005
=> d cost
COST IN U.S. DOLLARS
                                                 SINCE FILE
                                                                  TOTAL
                                                      ENTRY
                                                                SESSION
CONNECT CHARGES
                                                       0.00
                                                                  41.45
NETWORK CHARGES
                                                       0.60
                                                                   2.04
SEARCH CHARGES
                                                       0.00
                                                                 136.08
DISPLAY CHARGES
                                                       0.00
                                                                 47.98
                                                       ____
```

0.60

SINCE FILE

227.55

TOTAL

- (ii) when X is 3-7C alkyl or 3-7C alkenyl and R10-R12 are H, 1-10C halo upto perhaloalkyl, 1-10C alkyl, 3-12C cycloalkyl, 2-10C alkenyl, 5-7C cycloalkenyl or 3-10C alkynyl, then at least one T is NO2, CN, CF3 or halo;
- (iii) when R13 is 6-12C aryl, at least one T is NO2, CN, CF3 or halo; (iv) in (II), when NR15R16 form morpholine, the morpholine is substituted by R21 and/or R22, and
 - (v) when R20 is phenyl, one of R15 a R16 is R19-R20.

An INDEPENDENT CLAIM is included for treating diseases or conditions (see 'USE' section) which comprises administering a compound of formula (III) or (IV).

R26 = H, 1-10C alkyl, 1-10C halo upto perhaloalkyl, 3-12C cycloalkyl, heterocycloalkyl with 4-7C and 1-3 N, S and O heteroatoms, 2-10C alkenyl, 5-12C mono- to tri-cyclic cycloalkenyl, or 3-10C alkynyl;

X' = a group of formula (i);

n = 3-7;

p = 0-7;

R32-R34 = H, 1-10C halo upto perhaloalkyl, 1-10C alkyl, 3-12C cycloalkyl, 2-10C alkenyl, 5-7C cycloalkenyl or 3-10C alkynyl, or CR34 = 3-6C spiro ring, or

R34 + adjacent C atom to which it is attached = fused ring containing 3-7 and 4-14H atoms, or

R34 + C atom 2-4C atoms from attached C atom = fused ring containing 3-7 and 4-14H atoms;

R35 = 6-12C aryl or heteroaryl having 2-11C atoms and 1-3 N, S and O heteroatoms;

R36=6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O heteroatoms, 1-10C alkyl, 3-12C cycloalkyl, heterocyclylalkyl having 4-7C and 1-3 N, S and O heteroatoms, 2-10C alkenyl, 5-12C cycloalkenyl or R17-R18.

The proviso for T in (IV) does not apply.

ACTIVITY - Osteopathic; Contraceptive; Gynecological; Tocolytic; Analgesic; Nootropic; Antidepressant; Cardiant; Cytostatic; Depilatory. MECHANISM OF ACTION - Progesterone receptor (PR) modulator.

In a PR receptor binding assay for measuring inhibition of binding of tritiated progesterone to PR in T47D cell cytosol, N-(4-(2-ethylbutyl)-4-azatricyclo(4,3,1,138)undec-5-ylidene) -2-methyl-4-nitroaniline (Ia) inhibited 80-100% binding at 200 nM.

USE - Used for enhancing bone formation in bone weakening diseases for treating osteopenia or osteoporosis, fracture healing, recognition and maintenance of pregnancy, sensory and motor functions, short term memory and male and female sexual receptivity, preventing endometrial implantation, postsurgical adhesion formation and myocardial infarction, inducing labor, treating luteal deficiency, preecamplsia, eclampsia of pregnancy, preterm labor, infertility, dysmenorrhea, dysfunctional uterine bleeding, ovarian hyperandrogynism, ovarian hyperaldosteronism, premenstrual syndrome and tension, premenstrual behavior disorders, climeracteric disturbance, post menopausal urinary incontinence, postpartum depression, genital atrophy, cancers, endometriosis, uterine fibroids, hirsutism and hair growth, use as a female contragestive agent, regulating uterine immune function, hormone replacement, male contraception, abortion and promoting mylin repair

ADVANTAGE - The compounds have fewer side effects. Dwg.0/0

=> file stnguide		
COST IN U.S. DOLLARS	SINCE FILE	TOTAL
	ENTRY	SESSION
FULL ESTIMATED COST	226.29	226.95
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)	SINCE FILE	TOTAL
	ENTRY	SESSION
CA SUBSCRIBER PRICE	-5.84	-5.84

t = 1-5;R2 = 2-10C alkyl, 1-10C halo upto perhaloalkyl, 3-12C cycloalkyl, heterocycloalkyl with 4-7C and 1-3 N, S and O heteroatoms, 2-10C alkenyl, 5-12C mono- to tri-cyclic cycloalkenyl, or 3-10C alkynyl; G = H, NO2, CN, halo, OH, OR4, oxo, 1-4C halo upto perhaloalkyl, or 1-4C alkyl, 2-4C alkenyl, 3-7C cycloalkyl, heterocycloalkyl of 3-5 C and 1-3 N, O and S heteroatoms, 5-7C cycloalkenyl or heterocycloalkenyl of 4-6C and 1-3 N, O and S heteroatoms (all optionally substituted by at least 1 halo upto perhalo), COOR4, CONR5R6, or 6-10C aryl or heteroaryl of

alkyl and halo upto perhalo), S(O)yR7, SO3R7 or SO2NR5R6; R4 = 1-4C alkyl, 1-4C halo upto perhaloalkyl, 3-6C cycloalkyl or 3-6C halocycloalkyl;

3-9C and 1-3 N, O and S heteroatoms (both optionally substituted by 1-3

R5, R6 = H or 1-5C alkyl;

R7 = 1-5C alkyl, fluorosulfonyl, formyl, OH, CN, halo, N-oxide, OC(R8)20, CONHCO (with C atoms attached to adjacent positions on R) or CO-phenyl, attached to R ortho to the carbonyl;

R8 = H, halo or 1-4C alkyl;

y = 0-2;

g = 0-4, except where G is halo which may be present to perhalo level;

X = 3-7C alkyl or 3-7C alkenyl, or

X = a group forming a polycyclic 3-4 ring structure, each ring of 3-8C and optionally substituted by at least one 1-6C alkyl or 2-6C

R10-R12 = H, 1-10C halo upto perhaloalkyl, 1-10C alkyl, 3-12Ccycloalkyl, 2-10C alkenyl, 5-7C cycloalkenyl or 3-10C alkynyl, or

CR12 = 3-6C spiro ring, 3-7C and 4-14H fused ring or

R12 + the C atom 2-4C atoms from the attached C atom = a 3-7C and 4-14H fused ring;

R13 = 6-12C aryl or 4-pyridyl;

R14 = 6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O heteroatoms, 1-10C alkyl, 3-12C cycloalkyl, heterocyclylalkyl having 4-7C and 1-3 N, S and O heteroatoms, 2-10C alkenyl, 5-12C monocycloalkenyl or R17-R18;

R17 = 1-10C alkyl or 2-10C alkenyl;

R18 = 6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O heteroatoms, 3-12C cycloalkyl, heterocyclylalkyl having 4-7C and 1-3 N, S and O heteroatoms or 5-12C cycloalkenyl;

R15, R16 = H, 6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O heteroatoms, 1-10C alkyl, 3-12C cycloalkyl, heterocycloalkyl having 4-7Cand 1-3 N, S and O heteroatoms, 2-10C alkenyl, 5-12C cycloalkenyl or R19-R20, so that the total number of non H atoms on R14-R16 is at least 9,

NR15R16 = 5-8 membered ring containing 4-7C and 1 or 2 N, S and O heteroatoms (optionally substituted by R21 and R22); R19 = 1-10C alkyl, 3-12C cycloalkyl, heterocycloalkyl having 4-7C and

1-3 N, S and O heteroatoms, 2-10C alkenyl or 5-12C cycloalkenyl;

R20 = H, 6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O heteroatoms, 3-12C cycloalkyl, heterocycloalkyl having 4-7C and 1-3 N, S and O heteroatoms, 5-12C cycloalkenyl or R23-R24;

R23 = 6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O

R24 = H, halo, CN, NO2, 1-10C alkyl, 1-6C haloalkyl having 1-3 halo; R21, R22 = H, 1-10C halo upto perhaloalkyl, 1-10C alkyl, 6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O heteroatoms or benzimidazolinone, or

CR21 or CR22 = fused ring having 3-6C and 4-10H atoms, or R22 + adjacent C to which it is attached = fused ring having 3-6C and 4-10H atoms; provided that:

(i) when X is 3-4C alkyl and R10-R12 are H; t is 1; at least one T is 4-NO2 or 4-CN and at least one other T is 2-alkyl, 2-halo or 2-CF3, and R1 is phenyl;

RODRIGUEZ, M E; WANG, M; RODRIQUEZ, M E

PATENT ASSIGNEE(S): (FARB) BAYER CORP; (BULL-I) BULLOCK W H; (COLL-I)

COLLIBEE W L; (DALL-I) DALLY R; (KLUE-I) KLUENDER H C E;

(RODR-I) RODRIGUEZ M E; (WANG-I) WANG M

98

COUNTRY COUNT:
PATENT INFORMATION:

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ

NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO

RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001088529 A 20020322 (200251) BR 2001007179 A 20020702 (200252) CN 1395467 A 20030205 (200334)

EP 1317456 A2 20030611 (200339) EN

R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT

RO SE SI TR

ZA 2002003389 A 20030625 (200348) 143

US 2003229072 A1 20031211 (200382)

JP 2004508373 W 20040318 (200420) 225

APPLICATION DETAILS:

PAT	TENT NO	KIND	APPLICATION	DATE
WO	2002020526	A2	WO 2001-US27007	20010830
ΑU	2001088529	A	AU 2001-88529	20010830
BR	2001007179	A	BR 2001-7179	20010830
			WO 2001-US27007	20010830
CN	1395467	A	CN 2001-803536	20010830
EΡ	1317456	A2	EP 2001-968272	20010830
			WO 2001-US27007	20010830
ZA	2002003389	A	ZA 2002-3389	20020429
US	2003229072	A1	WO 2001-US27007	20010830
			US 2003-363621	20030303
JΡ	2004508373	W	WO 2001-US27007	20010830
			JP 2002-525147	20010830

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001088529 BR 2001007179 EP 1317456 JP 2004508373	A Based on A Based on A2 Based on W Based on	WO 2002020526 WO 2002020526 WO 2002020526 WO 2002020526

PRIORITY APPLN. INFO: US 2000-656854 20000907

ED 20020704

AN 2002-393837 [42] WPIDS

AB WO 200220526 A UPAB: 20030317

NOVELTY - Cyclic and acyclic amidine compounds (I) and (II) are new.

DETAILED DESCRIPTION - Cyclic amidine compounds of formula (I) and acyclic amidine compounds of formula (II) and their salts, are new.

R1 = 6-12C aryl or heteroaryl with 2-11 carbon and 1-3 N, O or S heteroatoms;

T = H, NO2, CN, 1-6C alkyl, 1-6C halo upto perhaloalkyl, 6-12C aryl or heteroaryl with 2-11 carbon and 1-3 N, O or S heteroatoms, or

T + adjacent C atom = a fused ring of 6-9 C and 4-14 hydrogen atoms;

function is reviewed. Finally, 1 potentially revolutionary therapeutic strategy that takes advantage of the important contribution of K+ channels and gap junctions to erectile physiol. is described: maxi-K ion channel (gene) therapy.

REFERENCE COUNT:

81 THERE ARE 81 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 19 OF 20 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

ACCESSION NUMBER: 2004123250 EMBASE

TITLE: EDHF: New therapeutic targets?.

AUTHOR: Feletou M.; Vanhoutte P.M.

CORPORATE SOURCE: M. Feletou, Dept. Diabete Maladies Metaboliques, Institut

de Recherches Servier, 11 rue des Moulineau, 92150

Suresnes, France. michel.feletou@fr.netgrs.com

SOURCE: Pharmacological Research, (2004) Vol. 49, No. 6, pp.

565-580. Refs: 244

ISSN: 1043-6618 CODEN: PHMREP

PUBLISHER IDENT.: S 1043-6618 (03) 00411-0

COUNTRY:

United Kingdom

DOCUMENT TYPE:

Journal; General Review

FILE SEGMENT: 005

General Pathology and Pathological Anatomy

030 Pharmacology

037 Drug Literature Index

LANGUAGE: English SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 20040412

Last Updated on STN: 20040412

ED Entered STN: 20040412

Last Updated on STN: 20040412

AΒ Besides cyclooxygenase and NO-synthase, another distinct endothelial pathway, endothelium-dependent hyperpolarization (EDHF), is involved in the relaxation of the vascular smooth muscle cells. EDHF has been demonstrated unequivocally in various blood vessels from different species, including human, and is likely to play an important role in cardiovascular physiology. This alternative pathway involves the activation of two populations of endothelial potassium channels, the small conductance and intermediate conductance

calcium-activated potassium channels (SK(Ca) and IK(Ca), respectively). EDHF-mediated responses are clearly altered in various pathological conditions (ageing, hypertension, atherosclerosis, hypercholesterolemia, heart failure, ischemiareperfusion, angioplasty, eclampsia, diabetes, sepsis). Therapeutic or adjutant interventions (angiotensin converting enzyme inhibitors, antagonist of the angiotensin receptor, estrogen, omega-3 polyunsaturated fatty acids, polyphenol derivatives, potassium and/or calcium intake) can restore these responses, suggesting that the improvement of the EDHF pathway contributes to the observed beneficial effect of these various substances. However, the improvement or restoration of EDHF responses has not been, yet, the direct purpose of any pharmaceutical effort. Activating endothelial IK(Ca) and/or SK(Ca) or increasing their expression as well as improving myo-endothelial communication, for instance by increasing the expression of connexin(s), could become interesting therapeutic targets. .COPYRGT. 2004 Elsevier Ltd. All rights reserved.

L30 ANSWER 20 OF 20 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER: 2002-393837 [42]

DOC. NO. CPI: C2002-110754

TITLE: New cyclic and acyclic amidine derivatives are

progesterone receptor modulators used for treating

osteoporosis and for fertility control.

WPIDS

DERWENT CLASS:

INVENTOR(S): BULLOCK, W H; COLLIBEE, W L; DALLY, R; KLUENDER, H C E;

Drugs of Today (2000), 36(2-3), 147-154 SOURCE:

CODEN: MDACAP; ISSN: 0025-7656

PUBLISHER: Prous Science

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English Entered STN: 21 Apr 2000

AB A review, with 42 refs. Decreased penile vascular resistance

induced by corporal smooth muscle relaxation is the most important step in penile erection. The heightened tone of the corporal

smooth muscles is considered a major cause in impotence. Modulation of corporal smooth muscle tone is a complex process requiring the integration of a host of intracellular events and extracellular signals. In intracellular events of corporal smooth muscle cell, the potassium channels and calcium channels play a major role. Functionally, potassium channels are important regulators of smooth muscle membrane potential in response to depolarizing stimuli and they counteract calcium channels. Potassium channels have been shown to play a fundamental role in both the physiol. and pathophysiol. regulation of smooth muscle tone in diverse tissues. Among the several subtypes of potassium channels, the calcium-sensitive (KCa) or maxi-K potassium channel subtypes are thought to be the most physiol. relevant in human corporal smooth muscle. Because of the physiol. role of maxi-K channels in human corporal smooth muscles, we investigated the maxi-K channels for the genetic therapy of erectile dysfunction. These data indicate that naked hSlo DNA of maxi-K channels is quite easily incorporated into corporal smooth muscle and expression of the maxi-K hSlo cDNA appeared to be

sustained for 1-4 mo postinjection. These results show the possibility of a similar genetic strategy of potassium channels in humans. THERE ARE 42 CITED REFERENCES AVAILABLE FOR THIS REFERENCE COUNT: 42

L30 ANSWER 18 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2000:312120 CAPLUS

DOCUMENT NUMBER: 133:159567

K+ channels and gap junctions in the modulation of TITLE:

corporal smooth muscle tone

AUTHOR(S): Christ, George J.

CORPORATE SOURCE: Depts. of Urology and Physiology and Biophysics,

Institute for Smooth Muscle Biology, Laboratory of Molecular and Integrative Urology, Albert Einstein

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

College of Medicine, Bronx, NY, 10461, USA Drug News & Perspectives (2000), 13(1), 28-36

CODEN: DNPEED; ISSN: 0214-0934

Prous Science PUBLISHER:

DOCUMENT TYPE: Journal; General Review

LANGUAGE: English Entered STN: 14 May 2000 ED

SOURCE:

A review with 81 refs. is given. Changes in the contractile status (i.e., AB contraction and relaxation) of corporal and arterial smooth muscle cells (myocytes) govern the flow of blood to and from the penis and, thus, ultimately have a major impact on erectile capacity. As with many other smooth muscle cell types, corporal myocyte contractility is inextricably linked to ion channel activity. Corporal smooth muscle cells possess a rich repertoire of ion channels, including Ca, Cl, and K channels, as well as gap junction (intercellular) channels. Among these, the KATP (i.e., the metabolically regulated K+ channel) and the KCa (i.e., maxi-K or large conductance, Ca-sensitive K+ channel) nonjunctional channel subtypes, as well as connexin43-derived gap junction (intercellular) channels, are thought to be particularly relevant to the control of corporal myocyte contractility. In fact, whereas K+ channels are an important convergence point for modulating cellular function, gap junctions are a major conduit for ensuring coordinated cellular, and thus tissue, function. The evidence documenting the presence and physiol. relevance of K+ channels and gap junctions to human erectile physiol. and

stimuli and kept in isometric organ bath immersed in a modified Krebs-Henseleit solution enriched with guanethidine and indomethacine were used in order to study the mechanism of the phentolamine-induced relaxation. Phentolamine caused relaxation (≈50%) in HCC strips precontracted with K+ 40 mM. This effect was not blocked by tetrodotoxin (1 μ M) (54.6 \pm 4.6 vs 48.9 \pm 6.4%) or (atropine (10 μ M) (52.7 \pm 6.5 vs 58.6 \pm 5.6%). However, this relaxation was significantly attenuated by L-NAME (100 μ M) (59.7 \pm 5.8 vs 27.8 \pm 7.1%; P<0.05; n=8) and ODQ (100 μ M) (62.7 \pm 5.1 vs 26.8 \pm 3.9%; P<0.05; n=8). Charybdotoxin and apamin (KCa-channel blockers) did not affect the phentolamine relaxations (54.6±4.6 vs 59.3±5.2%). Glibenclamide (100 μM), an inhibitor of KATP-channel, caused a significant inhibition $(56.7\pm6.3 \text{ vs } 11.3\pm2.3\%; \text{ P}<0.05; \text{ n}=8)$ of the phentolamine-induced relaxation. In addition, the association of glibenclamide and L-NAME almost abolished the phentolamine-mediated relaxation (54.6±5.6 vs 5.7 \pm 1.4%; P<0.05; n=8). The results suggest that phentolamine relaxes HCC by a nonadrenergic-noncholinergic mechanism dependent on nitric oxide synthase activity and activation of KATP-channel.

REFERENCE COUNT:

THERE ARE 27 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 16 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

27

ACCESSION NUMBER:

2004:816279 CAPLUS

DOCUMENT NUMBER:

142:168588

TITLE:

Potassium channel subtypes as molecular targets for overactive bladder and other urological disorders

AUTHOR(S):

Gopalakrishnan, Murali; Shieh, Char-Chang

CORPORATE SOURCE:

Neuroscience Research, Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL,

60064, USA

SOURCE:

Expert Opinion on Therapeutic Targets (2004), 8(5),

437-458

CODEN: EOTTAO; ISSN: 1472-8222

PUBLISHER:

Ashley Publications Ltd.

DOCUMENT TYPE:

Journal; General Review

LANGUAGE:

English

ED Entered STN: 07 Oct 2004

AB A review. Potassium channels have re-emerged as attractive targets for overactive bladder and other urol. diseases in recent years, in part due to an enhanced understanding of their mol. heterogeneity, tissue distribution, functional roles and regulation in physiol. and pathol. states. Cloning and heterologous expression anal., coupled with the advancement of improved high-throughput screening techniques, have enabled expeditious identification of selective small-mol. openers and blockers for ATP-sensitive K+ channels, Ca2+-activated K+ channels and voltage-dependent K+ channel-KQT-like subfamily (KCNQ) members, and has paved the way in the assessment of efficacy and adverse effects in preclin. models. This review focuses on the rationale for mol. targeting of K+ channels, the current status of target validation, including preclin. proof-of-concept studies, and provides perspectives on the limitations and hurdles to be overcome in realizing the potential of these targets for diverse urol. indications such as overactive bladder, erectile dysfunction and prostate diseases.

REFERENCE COUNT:

THERE ARE 216 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L30 ANSWER 17 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2000:256133 CAPLUS

DOCUMENT NUMBER:

133:56349

TITLE:

Physiological roles and properties of potassium

channels in corporal smooth muscle

AUTHOR(S):

Lee, Sung Won

CORPORATE SOURCE:

Albert Einstein College of Medicine, New York, NY, USA

channel modulators in treatment of

erectile dysfunction

INVENTOR(S): Maw, Graham Nigel; Wayman, Christopher Peter

Pfizer Limited, UK; Pfizer Inc. PCT Int. Appl., 120 pp. PATENT ASSIGNEE(S):

SOURCE:

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PA'	rent	NO.			KIN	D -	DATE			APPI	LICAT	ION 1	NO.		D.	ATE	
	2002 2002						2002		,	wo 2	2001-	IB15	25.		2	0010	824
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	R₩:	US, GH, DE,	UZ, GM, DK,	VN, KE, ES,	YU, LS, FI,	ZA, MW, FR,	ZW, MZ, GB,	AM, SD, GR,	AZ, SL, IE,	BY, SZ, IT,	, KG, , TZ, , LU,	KZ, UG, MC,	MD, ZW, NL,	RU, AT, PT,	TJ, BE, SE,	TM CH, TR,	CY,
AU	2420	852 0823	77		A A A 5		2002 2002	0307 0313		CA 2 AU 2	2001-: 2001-:	2420 8237	852 7		2	0010 0010	824
EP		AT,	BE,	CH,	DE,	DK,		FR,	GB,	GR,	2001- , IT, , TR						
		1850	94							US 2	2002- 2001- 2000-	9390	93		2	0010 0010 0000	824
											2000-: 2001-					0001 0010	

ED Entered STN: 08 Mar 2002

AΒ A method of treating an individual is described. The method comprise delivering to the individual an agent that is capable of modulating an intermediate conductance calcium-activated potassium (IKCa) channel in the sexual genitalia of the individual; wherein the modulation of the IKCa channel by the agent is capable of mediating a relaxation of corpus cavernosal smooth muscle tone. The agent may be admixed with a pharmaceutically acceptable carrier, diluent or excipient.

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L30 ANSWER 15 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN
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ACCESSION NUMBER:

2005:8889 CAPLUS

TITLE:

Phentolamine relaxes human corpus

cavernosum by a nonadrenergic mechanism

activating ATP-sensitive K+ channel

AUTHOR(S): Silva, L. F. G.; Nascimento, N. R. F.; Fonteles, M.

C.; de Nucci, G.; Moraes, M. E.; Vasconcelos, P. R.

L.; Moraes, M. O.

CORPORATE SOURCE:

Surgery Department, Federal University of Ceara,

Ceara, Brazil

SOURCE:

International Journal of Impotence Research (2005),

17(1), 27-32

CODEN: IJIRFB; ISSN: 0955-9930

PUBLISHER: DOCUMENT TYPE: Nature Publishing Group

Journal English

LANGUAGE:

Entered STN: 06 Jan 2005 AΒ

To investigate the pharmacodynamics of phentolamine in human corpus cavernosum (HCC) with special attention to the role of the K+ channels. Strips of HCC precontracted with nonadrenergic ACCESSION NUMBER:

2002:465801 CAPLUS

DOCUMENT NUMBER:

137:52344

TITLE:

Treatment of male sexual dysfunction

INVENTOR(S):

Naylor, Alasdair Mark; Van der Graaf, Pieter Hadewijn;

Wayman, Christopher Peter

PATENT ASSIGNEE(S):

Pfizer Limited, UK; Pfizer Inc.

SOURCE:

PCT Int. Appl., 179 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT:

10

PATENT INFORMATION:

ΕD Entered STN: 21 Jun 2002

The use of an inhibitor of a neuropeptide Y (NPY), preferably of a NPY Y1 AΒ receptor, which inhibitor is selective for an NPY or NPY Y1 receptor associated with male genitalia, in the preparation/manufacture of a medicament for the treatment or prevention of male erectile dysfunction (MED).

REFERENCE COUNT:

7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L30 ANSWER 14 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 4

ACCESSION NUMBER:

2002:171727 CAPLUS

DOCUMENT NUMBER:

136:210533

TITLE:

Intermediate conductance calcium-activated potassium Biophysical Society.

ISSN: 0006-3495 (ISSN print).

DOCUMENT TYPE:

Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

LANGUAGE:

English

ENTRY DATE: Entered STN: 3 Mar 2004

Last Updated on STN: 3 Mar 2004

ED Entered STN: 3 Mar 2004

Last Updated on STN: 3 Mar 2004

AB In some vascular muscles vasodilators increase activity of Ca2+-dependent K+ channels (KCa), regulating membrane potential and leading to relaxation. In corpus cavernosum (CC) smooth muscle, vasodilation leads to erection. CC cells exhibit both KCa and Ca2+-dependent Cl- channels (ClCa), although their precise role in regulation of membrane potential is unresolved. Both KCa and ClCa are spontaneously active, apparent as spontaneous transient outward (STOCS) and inward (STICS) currents, which are mediated by Ca2+ sparks - spontaneous release of Ca2+ through ryanodine receptors. Our aim was to

investigate the regulation of Ca2+ release from stores and its effect on Ca2+-dependent currents in CC smooth muscle. Single cells were isolated from rat CC, perforated patch clamp methods were used to record currents, and fluorescent dyes were used to monitor intracellular Ca2+ levels. Phenylephrine (PE) caused transient elevation of intracellular Ca2+ concentration accompanied by contraction. We tested the effects of the vasodilator, nitric oxide, on cytosolic Ca2+ and membrane currents in CC. Whereas treatment of cells with nitric oxide donors and sildenafil citrate, an inhibitor of phosphodiesterase 5, had no effect on basal Ca2+ levels, receptor-mediated rise of Ca2+ was significantly inhibited. Moreover, nitric oxide donors and sildenafil inhibited the receptor activation of KCa and ClCa currents. Down-regulation of this excitatory pathway represents a novel means for promoting relevation

excitatory pathway represents a novel means for promoting relaxation. Treatment of CC cells with nitric oxide donors and sildenafil reduced the frequency of STOCS and STICs, an effect that was mimicked by a cGMP analog. This is a second pathway that regulates release of Ca2+ from sarcoplasmic reticulum. Thus, we demonstrate two distinct pathways by which nitric oxide signaling dynamically regulates Ca2+ release from intracellular stores, and in turn modulates the activity of Ca2+-dependent channels in corpus cavernosum.

L30 ANSWER 12 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2000:203407 BIOSIS DOCUMENT NUMBER: PREV200000203407

TITLE: KCa channel current regulates membrane potentials

in freshly isolated human corporal smooth muscle cells.

AUTHOR(S): Wang, Hong-Zhan [Reprint author]; Christ, George J.

[Reprint author]

CORPORATE SOURCE: New York, NY, USA

SOURCE: Journal of Urology, (April, 2000) Vol. 163, No. 4 Suppl.,

pp. 207. print.

Meeting Info.: 95th Annual Meeting of the American

Urological Association, Inc. Atlanta, Georgia, USA. April

29, 2000-May 04, 1999.

CODEN: JOURAA. ISSN: 0022-5347.

DOCUMENT TYPE: Conference; (Meeting)

Conference; Abstract; (Meeting Abstract)

Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 24 May 2000

Last Updated on STN: 5 Jan 2002

ED Entered STN: 24 May 2000

Last Updated on STN: 5 Jan 2002

L30 ANSWER 13 OF 20 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 3

L30 ANSWER 10 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on

STN

ACCESSION NUMBER: 2004:278292 BIOSIS DOCUMENT NUMBER: PREV200400279104

TITLE: Role of ATP-sensitive K+ channels in relaxation of

penile resistance arteries.

AUTHOR(S): Rubio, Jose L. Ruiz; Hernandez, Medardo; de los Arcos, Luis

Rivera; Benedito, Sara; Recio, Paz; Garcia, Pilar;

Garcia-Sacristan, Albino; Prieto, Dolores [Reprint Author]

CORPORATE SOURCE: Fac FarmDept Fisiol, Univ Complutense Madrid, Madrid,

28040, Spain

SOURCE: Urology, (April 2004) Vol. 63, No. 4, pp. 800-805. print.

ISSN: 0090-4295 (ISSN print).

DOCUMENT TYPE: Article LANGUAGE: English

ENTRY DATE: Entered STN: 9 Jun 2004

Last Updated on STN: 9 Jun 2004

ED Entered STN: 9 Jun 2004

Last Updated on STN: 9 Jun 2004

AB Objectives. To investigate the functional presence of adenosine triphosphate (ATP)-sensitive potassium (K+) channels (KATP) in penile resistance arteries by evaluating the relaxant effects of the selective KATP channel openers, cromakalim and levcromakalim, and also the involvement of KATP channels in the relaxation of two drugs currently used in the treatment of erectile dysfunction (ie,

prostaglandin E1 (PGE1) and sildenafil). Methods. Penile resistance arteries were dissected from the horse corpus

cavernosum and mounted in microvascular myographs for isometric tension recording. The arteries were precontracted with phenylephrine, and the responses to several vasodilators were tested in the absence and presence of K+ channel blockers. Results. Cromakalim and levcromakalim evoked complete concentration-de pendent relaxations that were blocked by 3 mum of the selective KATP channel inhibitor glibenclamide. Raising extracellular K+ (25 mM) inhibited the relaxations to PGE1 and to the selective inhibitor of the cyclic adenosine monophosphate-specific phosphodiesterase (PDE4) rolipram. At a concentration selective for calcium-activated K+(Kca) channels (3 mM), tetraethylammonium inhibited rolipram responses but not those of PGE1. However, glibenclamide significantly reduced the relaxation to both PGE1 and rolipram, but not those induced by the selective inhibitor of the type 5 cyclic guanosine monophosphate-specific phosphodiesterase (PDE5). Conclusions. The present results suggest a functional role for KATP channels in the relaxation of penile resistance arteries, as well as their differential involvement in the vasodilation to drugs used in the treatment of organic erectile dysfunction.

They mediated relaxation to PGE1 and cyclic adenosine monophosphateelevating agents, but not those of cyclic guanosine monophosphateelevating agents such as sildenafil.

L30 ANSWER 11 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:122655 BIOSIS DOCUMENT NUMBER: PREV200400126538

TITLE: Nitric oxide regulates Ca2+-dependent currents in

corpus cavernosum smooth muscle through

two distinct mechanisms.

AUTHOR(S): Williams, Beatrice A. [Reprint Author]; Liu, Ciaqiong [Reprint Author]; Sims, Stephen M. [Reprint Author]

CORPORATE SOURCE: Physiology and Pharmacology, University of Western Ontario,

London, ON, Canada

SOURCE: Biophysical Journal, (January 2004) Vol. 86, No. 1, pp.

104a. print.

Meeting Info.: 48th Annual Meeting of the Biophysical Society. Baltimore, MD, USA. February 14-18, 2004.

cavernosum and mounted in microvascular myographs in order to investigate the mechanisms underlying the endothelium-dependent relaxations to acetylcholine (ACh) and bradykinin (BK). 2. In arteries preconstricted with the thromboxane analogue U46619 (3-30 nM), ACh and BK elicited concentration-dependent relaxations, pD2 and maximal responses being 7.71 +- 0.09 and 91 +- 1% (n = 23), and 8.80 +- 0.07 and 89 +- 2% (n = 24) for ACh and BK, respectively. These relaxations were abolished by mechanical endothelial cell removal, attenuated by the nitric oxide (NO) synthase (NOS) inhibitor, NG-nitro-L-arginine (L-NOARG, 100 mum) and unchanged by indomethacin (3 muM). However, raising extracellular K+ to concentrations of 20-30 mM significantly inhibited the ACh and BK relaxant responses to 63+-4% (P<0.01, n=7) and to 59+4% (P<0.01, n=6), respectively. ACh- and BK-elicited relaxations were abolished in arteries preconstricted with K+ in the presence of 100 muM L-NOARG. 3. In contrast to the inhibitor of ATP-sensitive K+ channels, the blockers of Ca2+-activated K+ (KCa) channels, charybdotoxin (30 nM) and apamin (0.3 muM), each induced slight but significant rightward shifts of the relaxations to ACh and BK without affecting the maximal responses. Combination of charybdotoxin and apamin did not cause further inhibition of the relaxations compared to either toxin alone. In the presence of L-NOARG (100 muM), combined application of the two toxins resulted in the most effective inhibition of the relaxations to both ACh and BK. Thus, pD2 and maximal responses for ACh and BK were 7.65 +- 0.08 and 98 +- 1%, and 9.17 +- 0.09 and 100 +- 0%, respectively, in controls, and 5.87 +-0.09 (P < 0.05, n = 6) and 38 +- 11% (P < 0.05, n = 6), and 8.09 +- 0.14 (P < 0.01, n = 6) and 98 +- 1% (n = 6), respectively, after combined application of charybdotoxin plus apamin and L-NOARG. 4. The selective inhibitor of guanylate cyclase, 1H-(1,2,4)oxadiazolo(4,3-a)quinoxalin-1one (ODQ, 5 muM) did not alter the maximal responses to either ACh or BK, but slightly decreased the sensitivity to both agonists, deltapD2 being 0.25+-0.07 (P<0.05, n = 6) and 0.62+-0.12 (P<0.01, n = 6) for ACh and BK, respectively. Combined application of ODQ and charybdotoxin plus apamin produced further inhibition of the sensitivity to both ACh (deltapD2 = 1.39+-0.09, P<0.01, n = 6) and BK (1.29+-0.11, P<0.01, n=6), compared to either ODQ or charybdotoxin plus apamin alone. 5. Exogenous nitric oxide (NO) present in acidified solutions of sodium nitrite (NaNO2) and S-nitroso-cysteine (SNC) both concentration-dependently relaxed penile resistance arteries, pD2 and maximal responses being 4.84 +- 0.06 and 82 +- 3% (n = 12), and 6.72 +- 0.07 and 85 +- 4% (n = 19), respectively. Charybdotoxin displaced to the right the dose-relaxation curves for both NO (deltapD2 0.38+-0.06, P<0.01, n = 6) and SNC (deltapD2 0.50+-0.10, P<0.01, n = 5), whereas apamin only reduced sensitivity (deltapD2 = 0.35+-0.12, P<0.05, n = 5) and maximum response (65+-9%, 1)P<0.05, n=6) to SNC. ODQ shifted to the right the dose-relaxation curves to both NO and SNC. The relaxant responses to either NO or SNC were not further inhibited by a combination of ODQ and charybdotoxin or ODQ and charybdotoxin plus apamin, respectively, compared to either blocker alone. 6. In the presence of 3 muM phentolamine, 5 muM ouabain contracted penile resistance arteries by 50 +- 6% (n = 17) of K-PSS, but did not significantly change the relaxant responses to either ACh, BK or NO. However, in the presence of L-NOARG ouabain reduced the ACh- and BK-elicited relaxation from 94+-3% to 16+-5% (P<0.0001, n=6), and from 98+-2% to 13+-3% (P<0.0001, n = 5), respectively. Combined application of ODQ and ouabain inhibited the relaxations to NO from 92+-2% to 26+-3% (P < 0.0001, n = 6). 7. The present results demonstrate that the endothelium-dependent relaxations of penile small arteries involve the release of NO and a non-NO non-prostanoid factor(s) which probably hyperpolarize(s) smooth muscle by two different mechanisms: an increased charybdotoxin and apamin-sensitive K+ conductance and an activation of the Na+-K+ATPase. These two mechanisms appear to be independent of guanylate cyclase stimulation, although NO itself can also activate charybdotoxin-sensitive K+ channels and the Na+-K+ pump through both cyclic GMP-dependent and independent mechanisms, respectively.

ED Entered STN: 19950404

Last Updated on STN: 19980206 Entered Medline: 19950320

AΒ Previous studies have demonstrated that cultured corporal smooth muscle cells have prominent outward K currents composed of several different K channel subtypes. The goals of the present investigation were (1) to assert the nature of these channels and to evaluate the characteristics of the most predominant of these channel subtypes, the Maxi-K+ (KCa) channel, and (2) to compare KCa channel behavior in cultured corporal smooth muscle cells derived from the human corpus cavernosum of two distinct patient populations. The patient population was subdivided into two broad diagnostic categories: Group 1: 4 patients without evidence of organic disease of the corpus cavernosum, 3 of whom had documented erections; and Group 2: 4 patients with organic erectile dysfunction. Consistent with previous observations, 3 different K channel subtypes were detected in both patient populations, with corresponding conductances of 180, 100 and 40 pS, respectively. The approximately 183 pS channel was identified as the KCa channel based on its selective permeability to K+ and the fact that its open probability was modulated by both membrane potential and intracellular calcium levels. Specifically, the relative permeability of the 183 pS KCa channel to K+, Rb+, and NH4+ was 1.00:0.64:0.46. The channel was virtually impermeable to Na+ and Li+ (relative permeability < 0.02). In addition, the KCa channel was responsible for more than 90% of the outward K+ current passed through the cell membrane when depolarized. Furthermore, pharmacological studies using the K channel blocker tetraethylammonium ion (TEA) revealed that the sensitivity of KCa channels to TEA inhibition (as judged by the [TEA] required to block one-half of the outward whole cell current induced by a 90 mV depolarizing pulse) in cells from Group 1 patients was 1.05 ± -0.22 mM. (n = 10 cells), while in sharp contrast the observed value for cells from Group 2 patients was 12.7 + - 3.8 (n = 9 cells). The difference between the two groups was highly significant. These observations confirm and extend our previous studies to suggest that the KCa channel plays an important role in corporal smooth muscle physiology and, moreover, that alterations in the function/regulation of KCa channels may be an important feature of organic erectile dysfunction. As such, altered KCa channel behavior may contribute to an impaired hyperpolarizing ability of corporal smooth muscle, possibly altering intracellular calcium homeostasis and, perhaps, corporal smooth muscle reactivity and tone.

L30 ANSWER 9 OF 20 BIOSIS COPYRIGHT (c) 2005 The Thomson Corporation on STN

DUPLICATE 7

ACCESSION NUMBER: 1998:261488 BIOSIS DOCUMENT NUMBER: PREV199800261488

DOCUMENT NUMBER: PREV199800261488
TITLE: Contribution of K+

Contribution of K+ channels and ouabain-sensitive mechanisms to the endothelium-dependent relaxations of

horse penile small arteries.

AUTHOR(S): Prieto, Dolores [Reprint author]; Simonsen, Ulf; Hernandez,

Medardo; Garcia-Sacristan, Albino

CORPORATE SOURCE: Dep. Fisiologia, Fac. Veterinaria, Univ. Complutense,

28040-Madrid, Spain

SOURCE: British Journal of Pharmacology, (April, 1998) Vol. 123,

No. 8, pp. 1609-1620. print. CODEN: BJPCBM. ISSN: 0007-1188.

DOCUMENT TYPE:

Article English

LANGUAGE: ENTRY DATE:

Entered STN: 9 Jun 1998

Last Updated on STN: 12 Aug 1998

ED Entered STN: 9 Jun 1998

Last Updated on STN: 12 Aug 1998

AB 1. **Penile** small arteries (effective internal lumen diameter of 300-600 mum) were isolated from the horse **corpus**

journal of the International Society for Impotence

Research, (1999 Aug) 11 (4) 189-99. Journal code: 9007383. ISSN: 0955-9930.

PUB. COUNTRY:

ENGLAND: United Kingdom

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

199910

ENTRY DATE:

Entered STN: 19991101

Last Updated on STN: 19991101 Entered Medline: 19991020

ED Entered STN: 19991101

Last Updated on STN: 19991101 Entered Medline: 19991020

AB The large conductance calcium-sensitive potassium channel (KCa or maxi-K) is an important modulator of human corporal smooth muscle tone. and therefore, erectile capacity. The goal of this investigation was to evaluate the actions of prostaglandin El (PGE1), the most widely used and effective drug for the treatment of impotence, on the activity of the KCa channel, a prominent K+ current present in human corporal smooth muscle. Whole-cell patch clamp studies conducted on short-term cultured and enzymatically dissociated human corporal smooth muscle cells, revealed mean resting potentials of -50.8 +/- 2.1 mV (n = 8) and -34 +/- 4 mV (n = 8), respectively. In the attached-patch configuration, the corresponding single-channel slope conductance values for the KCa channel subtype were 173 +/-4 pS (n = 8) in cultured cells, and 190 +/- 13 pS (n = 3) in freshly isolated myocytes. Furthermore, voltage clamp experiments revealed that relative to control values, the application of PGE1 to cultured cells (3.3 or 33 microM) elicited an apparent increase in both the open probability (Po; ranging from 1.2-23 fold), and the mean open time (5-6 fold) of the KCa channel at membrane potentials of +90 mV and +110 mV. PGE1-induced alterations in KCa channel activity were also observed in freshly isolated corporal myocytes. In the whole cell-recording mode, statistically significant, Charybdotoxin-sensitive (100 nM) 2-3 fold increases in the outward K+ currents were observed in both cultured and freshly isolated corporal myocytes. The presence of a PKA inhibitor (fragment 6-22 amide; 10 microM) in the pipette tip was also associated with a nearly complete ablation of the observed PGE1-induced whole cell K+ currents. Taken together, these data confirm and extend our previous observations, and indicate that PGE1-induced relaxation of human corporal smooth muscle is related, at least in part, to activation of the KCa channel subtype resulting in cellular hyperpolarization.

L30 ANSWER 8 OF 20 MEDLINE on STN ACCESSION NUMBER: 95165564 MEDLINE DOCUMENT NUMBER: PubMed ID: 7861546

TITLE:

An analysis of the Maxi-K+ (KCa) channel in cultured human corporal smooth muscle cells.

AUTHOR:

Fan S F; Brink P R; Melman A; Christ G J

CORPORATE SOURCE:

Department of Urology, Albert Einstein College of

Medicine/Montefiore Medical Center, Bronx, New York 10461.

CONTRACT NUMBER: DK42027 (NIDDK)

HL31299 (NHLBI)

SOURCE:

Journal of urology, (1995 Mar) 153 (3 Pt 1) 818-25.

Journal code: 0376374. ISSN: 0022-5347.

PUB. COUNTRY:

United States

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Abridged Index Medicus Journals; Priority Journals

ENTRY MONTH: 199503

ENTRY DATE:

Entered STN: 19950404

Last Updated on STN: 19980206 Entered Medline: 19950320 ACCESSION NUMBER: 2001009814 MEDLINE DOCUMENT NUMBER: PubMed ID: 10953393

TITLE: [Bladder and cavernous contractility and relaxation among

intracellular messengers, changes in sarcoplasmatic free

calcium and phosphodiesterase activity].

Contrattilita e rilassamento vescicale e cavernoso tra messaggeri intracellulari, variazioni del calcio libero

sarcoplasmatico e attivita fosfodiesterasica.

AUTHOR: Alberti C

CORPORATE SOURCE: Libero Docente di Semeiotica Chirurgica, Universita degli

Studi di Parma.

SOURCE: Archivio italiano di urologia, andrologia : organo

ufficiale [di] Societa italiana di ecografia urologica e nefrologica / Associazione ricerche in urologia, (2000 Jun)

72 (2) 75-82. Ref: 37

Journal code: 9308247. ISSN: 1124-3562.

PUB. COUNTRY: Italy

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

(REVIEW, TUTORIAL)

LANGUAGE: Italian

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200010

ENTRY DATE: Entered STN: 20010322

Last Updated on STN: 20010322 Entered Medline: 20001026

ED Entered STN: 20010322

Last Updated on STN: 20010322 Entered Medline: 20001026

AΒ During the last decade, the cellular pathways involved in excitation-contraction coupling have been identified and explained. The key event in the initiation of the contraction is the rise in sarcoplasmic free calcium. Inositol 1,4,5-triphosphate (IP3) and cyclic nucleotides (cAMP, cGMP) have been demonstrated to be the second messengers associated with stimulation of smooth muscle selective receptor-subtypes (cholinergic, adrenergic, non adrenergic-non cholinergic) by specific neuromodulators. Furthermore, activation of voltage-gated L type- or receptor operated calcium channels is involved in the sarcoplasmic free calcium changes. KCa and KATP-channels play an important role in smooth muscle hyperpolarization; KATP-openers excite great interest as therapeutic agents for the detrusor instability. The specificity of different receptor subtypes and their transductional pathways has increased the number of targets for drug treatment of urinary bladder disorders and erectile dysfunction. As the level of intracellular nucleotide second messengers can be modulated by tissue-specific phosphodiesterase (PDE) isoenzymes, PDEs selective inhibitors have the potential to exert organ-specific therapeutic effects. So, PDE I selective inhibitor vinpocetine has been proposed for the symptomatic treatment of detrusor instability; PDE V selective inhibitor sildenafil, enhancing the NO-cGMP pathway-mediated cavernosal smooth muscle relaxation, is an effective drug to treat erectile dysfunction.

L30 ANSWER 7 OF 20 MEDLINE on STN ACCESSION NUMBER: 1999396849 MEDLINE DOCUMENT NUMBER: PubMed ID: 10467518

TITLE: Prostaglandin El activates the large-conductance

KCa channel in human corporal smooth muscle cells.

AUTHOR: Lee S W; Wang H Z; Zhao W; Ney P; Brink P R; Christ G J

CORPORATE SOURCE: Department of Urology, Sungkyunkwan University, College of

Medicine, Seoul, Korea.

CONTRACT NUMBER: DK42027 (NIDDK)

DK46379 (NIDDK)

SOURCE: International journal of impotence research : official

physiologically diverse organs. Intercellular communication through connexin43-derived gap junction channels and K+ flux through the KCa and KATP channel subtypes, in particular, appear to play prominent roles in this process. The goal of this report, therefore, is to review the data concerning junctional and nonjunctional ion channels on the detrusor myocytes of the urinary bladder, as well as on the specialized vascular myocytes of the corpus cavernosum

The choice of an excitable (i.e., bladder detrusor myocytes) and nonexcitable (i.e., corporal smooth muscle) smooth muscle cell type ensures that the discussion will at least encompass consideration of a large portion of the spectrum of physiological possibilities for the participation of junctional and nonjunctional ion channels in the initiation, maintenance and modulation of smooth muscle tone. A central thesis of this communication is that detailed knowledge of the myocyteand tissue-specific properties of K+ channels and gap junctions will likely lead to the improved understanding and treatment of human smooth muscle diseases/disorders.

L30 ANSWER 5 OF 20 MEDLINE on STN DUPLICATE 8

ACCESSION NUMBER: 94117302 MEDLINE DOCUMENT NUMBER: PubMed ID: 7507099

TITLE: Characterization of K currents in cultured human corporal

smooth muscle cells.

AUTHOR: Christ G J; Spray D C; Brink P R

CORPORATE SOURCE: Department of Urology, Albert Einstein College of

Medicine/Montefiore Medical Center, Bronx, New York 10461.

CONTRACT NUMBER: DK42027 (NIDDK)

HL31299 (NHLBI) NS07512 (NINDS)

SOURCE: Journal of andrology, (1993 Sep-Oct) 14 (5) 319-28.

Journal code: 8106453. ISSN: 0196-3635.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199402

ENTRY DATE: Entered STN: 19940312

Last Updated on STN: 19990129

Entered Medline: 19940224

ED Entered STN: 19940312

Last Updated on STN: 19990129 Entered Medline: 19940224

AΒ In order to gain more mechanistic insight into the regulation of corporal smooth muscle tone, we conducted electrophysiological studies on homogeneous explant cell cultures of human corpus cavernosum smooth muscle. Patch clamp analyses in the whole cell mode revealed a mean resting potential of -43 +/- 4.9 m V (n = 12 cells). Large whole cell outward K currents were very prominent in these cells, and ranged from 0.5 to 1.5 nA. In some cells, a transient, voltage-dependent A current accounted for a significant portion of the observed whole cell currents. Furthermore, stimulation with the calcium channel agonist BAY K 8644 or the K channel agonist pinacidil doubled the magnitude of the whole cell K current, as would be expected for maxi-K (KCa) and metabolically gated K channels (KATP), respectively. Single channel recordings in the detached patch mode consistently revealed the presence of at least two K channels: 1) a KCa channel, with a conductance of approximately 190 pS; and 2) a putative delayed rectifier channel with a conductance of approximately 50 pS. Furthermore, all channel types showed some degree of voltage and/or calcium sensitivity. In conclusion, the large magnitude of the whole cell K currents and the observed K channel heterogeneity indicate a potentially important role for these channels in modulating corporal smooth muscle tone.

smooth muscle tone. The purpose of this study was to investigate the effects of nitric oxide (NO) and sildenafil on the KCa channels and elucidate the mechanisms of action on the KCa channels in smooth muscle cells of the human corpus cavernosum. The conventional patch-clamp technique was applied to short-term cultured smooth muscle cells of the human corpus cavernosum. Single-channel currents were recorded in cell-attached or inside-out patches, and whole-cell currents were recorded in perforated-patches. cell-attached patches, sildenafil alone did not activate the KCa channels but sildenafil enhanced the NO-induced activation of KCa channels. The open probability of KCa channels was increased significantly after application of NO donor, SIN-1 (100 microM) (47 +/-7.1%, n = 10, P=0.002). The application of sildenafil (100 nM) with SIN-1 (100 microM) markedly increased the open probability of KCa channels (148 +/- 24%, n = 8, P < 0.001). The activation by SIN-1 or sildenafil with SIN-1 was completely blocked by pretreatment of the soluble guanylate cyclase inhibitor, ODQ (10 microM). In inside-out patches. SIN-1 or sildenafil with SIN-1 failed to activate KCa channels at pCa 7.5 (n=5). SIN-1 increased the whole cell outward K+ currents in all holding potential. The increased IK by SIN-1 was inhibited by charybdotoxin (CTX) about 70%. These data provide compelling evidence consistent with the involvement of the KCa channel subtype in modulating NO-induced relaxation responses in human corporal smooth muscle. Furthermore, the activation of KCa channels is thought to be mediated by activation of soluble quanylate cyclase, leading to increased intracellular levels of cyclic GMP and the subsequent activation of protein kinase rather than direct NO effect.

L30 ANSWER 4 OF 20 ACCESSION NUMBER:

MEDLINE on STN

DUPLICATE 6

DOCUMENT NUMBER:

2001416455 MEDLINE PubMed ID: 11465535

TITLE:

Physiological roles for K+ channels and gap junctions in

urogenital smooth muscle: implications for improved

understanding of urogenital function, disease and therapy.

AUTHOR:

Karicheti V; Christ G J

CORPORATE SOURCE:

Dept of Urology, Albert Einstein College of Medicine,

Bronx, NY 10461, USA.

SOURCE:

Current drug targets, (2001 Mar) 2 (1) 1-20. Ref: 136

Journal code: 100960531. ISSN: 1389-4501.

PUB. COUNTRY:

Netherlands

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

General Review; (REVIEW)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

200108

ENTRY DATE:

Entered STN: 20010813

Last Updated on STN: 20010813 Entered Medline: 20010809

ED Entered STN: 20010813

Last Updated on STN: 20010813 Entered Medline: 20010809

AB Smooth muscle cells constitute a heterogeneous collection of effector cells that, by virtue of both their constituency in blood vessels and presence as primary parenchymal cells in diverse tissues, affect the function of all organs. Thus, perhaps it is not surprising that alterations in, and/or dysfunction of, smooth muscle cells are quite common, and responsible, at least in part, for the morbidity and mortality associated with a very wide range of human diseases. These facts point to the necessity for improved understanding of the mechanism(s) governing the control of myocyte contractility (i.e., tone). Such understanding has been rapidly forthcoming in recent years, and has indicated that in many smooth muscle cell types intercellular communication through gap junctions acts in concert with nonjunctional (K+) ion channels to make important contributions to the control of myocyte tone and tissue homeostasis in

ED Entered STN: 20030812

Last Updated on STN: 20040512 Entered Medline: 20040511

AB The present study was designed to investigate the functional K+ channels involved in contractions induced by electrical field stimulation in isolated rat penile arteries. Blockers of Ca2+-activated K+ channels (KCa), tetraethylammonium, and of large-conductance KCa channels, charybdotoxin and iberiotoxin, as well as a blocker of voltage-dependent K+ channels (KV), 4-aminopyridine, increased resting tension in penile small arteries. In the presence of propranolol and NG-nitro-L-arginine (L-NOARG), electrical field stimulation evoked prazosin-sensitive contractions. In endothelium-intact preparations, these latter contractions were enhanced in the presence of tetraethylammonium and charybdotoxin. However, these blockers did not enhance contractions evoked by exogenously added noradrenaline. Endothelial cell removal increased the neurogenic contractions but tetraethylammonium had no further potentiating effect in these preparations. In the presence of an inhibitor of cyclooxygenase, indomethacin, and inhibitor of nitric oxide (NO) synthase, L-NOARG, acetylcholine evoked relaxations, which were abolished in the presence of either tetraethylammonium or charybdotoxin. In phenylephrine-contracted arteries treated with guanethidine and atropine, electrical field stimulation evoked relaxations, which were partially inhibited by L-NOARG and tetraethylammonium, without any additive effect of these drugs. These observations suggest that both large-conductance KCa channels and KV channels sensitive to iberiotoxin/tetraethylammonium and 4-aminopyridine, respectively, are directly involved in the modulation of myogenic tone of rat penile arteries. Furthermore, activation of endothelial intermediate-conductance KCa channels sensitive to tetraethylammonium and charybdotoxin leads to release of a non-NO nonprostanoid factor, which inhibits release of the neurotransmitter, noradrenaline, but these channels do not appear to be involved in inhibition of contraction evoked by exogenously applied noradrenaline in rat penile arteries.

L30 ANSWER 3 OF 20 MEDLINE on STN DUPLICATE 5

ACCESSION NUMBER: 2002035298

DOCUMENT NUMBER: PubMed ID: 11762799

TITLE: Effects of nitric oxide on the Ca2+-activated potassium

MEDLINE

channels in smooth muscle cells of the human corpus

cavernosum.

AUTHOR: Lee S W; Kang T M

CORPORATE SOURCE: Department of Urology, Samsung Medical Center, Sungkyunkwan

University School of Medicine, Seoul, Korea...

drswlee@smc.samsung.co.kr

SOURCE: Urological research, (2001 Oct) 29 (5) 359-65.

Journal code: 0364311. ISSN: 0300-5623. Germany: Germany, Federal Republic of Journal; Article; (JOURNAL ARTICLE)

DOCUMENT TYPE: Journal, LANGUAGE: English

PUB. COUNTRY:

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200205

ENTRY DATE: Entered STN: 20020124

Last Updated on STN: 20020508 Entered Medline: 20020507

ED Entered STN: 20020124

Last Updated on STN: 20020508 Entered Medline: 20020507

AB Relaxation of the corpus cavernosum smooth muscle is an absolute prerequisite of penile erection.

Potassium channels play a role in the physiologic regulation of corporal smooth muscle tone. Among the several subtypes of potassium channels, Ca2 +-activated potassium channel (KCa channel) subtypes are thought to be the most physiologically relevant in the regulation of corporal

R&D, Gunnels Wood Road, Stevenage, Hertfordshire, SG1 2NY,

UK.. mark.x.chen@gsk.com

SOURCE:

Naunyn-Schmiedeberg's archives of pharmacology, (2004 Jun)

369 (6) 602-15. Electronic Publication: 2004-05-01.

Journal code: 0326264. ISSN: 0028-1298. Germany: Germany, Federal Republic of Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

PUB. COUNTRY:

DOCUMENT TYPE:

Priority Journals

ENTRY MONTH:

200502

ENTRY DATE:

Entered STN: 20040616

Last Updated on STN: 20050223 Entered Medline: 20050222

ED Entered STN: 20040616

Last Updated on STN: 20050223 Entered Medline: 20050222

AΒ The SK/IK family of small and intermediate conductance

calcium-activated potassium channels

contains four members, SK1, SK2, SK3 and IK1, and is important for the regulation of a variety of neuronal and non-neuronal functions. In this study we have analysed the distribution of these channels in human tissues and their cellular localisation in samples of colon and corpus cavernosum. SK1 mRNA was detected almost exclusively in neuronal tissues. SK2 mRNA distribution was restricted but more widespread than SK1, and was detected in adrenal gland, brain, prostate, bladder, liver and heart. SK3 mRNA was detected in almost every tissue examined. It was highly expressed in brain and in smooth muscle-rich tissues including the clitoris and the corpus cavernosum, and

expression in the corpus cavernosum was upregulated up to 5-fold in patients undergoing sex-change operations. IK1 mRNA was present in surface-rich, secretory and inflammatory cell-rich tissues, highest in the trachea, prostate, placenta and salivary glands. detailed immunohistochemical studies of the colon and the corpus cavernosum, SK1-like immunoreactivity was observed in the enteric neurons. SK3-like immunoreactivity was observed strongly in smooth muscle and vascular endothelium. IK1-like immunoreactivity was mainly observed in inflammatory cells and enteric neurons of the colon, but absent in corpus cavernosum. These distinctive patterns of

distribution suggest that these channels are likely to have different biological functions and could be specifically targeted for a number of human diseases, such as irritable bowel syndrome, hypertension and erectile dysfunction.

L30 ANSWER 2 OF 20 MEDLINE on STN ACCESSION NUMBER:

2003374905 MEDLINE

DOCUMENT NUMBER:

CORPORATE SOURCE:

PubMed ID: 12909201

TITLE:

Ca2+-activated K+ channels in the endothelial cell layer involved in modulation of neurogenic contractions in rat

DUPLICATE 2

penile arteries.

AUTHOR:

Kun Attila; Martinez Ana Cristina; Tanko Laszlo B;

Pataricza Janos; Papp Julius Gy; Simonsen Ulf

Department of Pharmacology, University of Aarhus, 8000 Aarhus C, Denmark.

SOURCE:

European journal of pharmacology, (2003 Aug 1) 474 (1)

103-15.

Journal code: 1254354. ISSN: 0014-2999.

PUB. COUNTRY:

Netherlands

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

200405

ENTRY DATE:

Entered STN: 20030812

Last Updated on STN: 20040512 Entered Medline: 20040511

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FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 12:08:44 ON 14
     APR 2005
L18
            487 S (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANNEL
          63399 S (SEXUAL DYSFUNCTION? OR SEXUAL DISFUNCTION? OR ERECTILE DYSFU
L19
           1658 S (FEMALE SEXUAL DYSFUNCTION? OR FEMALE SEXUAL DISFUNCTION? OR
L20
           1081 S BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO"
L21
L22
          63430 S L19 OR L20
L23
         343217 S CLITOR? OR GENITAL? OR SEXUAL GENITAL? OR PENIS? OR PENILE? O
         381006 S L22 OR L23
L24
L25
             10 S L24 AND (L18 OR L21)
L26
              6 DUP REM L25 (4 DUPLICATES REMOVED)
=> d cost
COST IN U.S. DOLLARS
                                                 SINCE FILE
                                                                  TOTAL
                                                      ENTRY
                                                               SESSION
CONNECT CHARGES
                                                       30.27
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NETWORK CHARGES
                                                       0.96
                                                                   1.08
SEARCH CHARGES
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DISPLAY CHARGES
                                                      15.77
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FULL ESTIMATED COST
                                                     166.07
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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
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                                                                  TOTAL
                                                      ENTRY
                                                                SESSION
CA SUBSCRIBER PRICE
                                                       -1.46
                                                                  -1.46
IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' AT 12:17:54 ON 14 APR 2005
=> s ((intermediate conductance) (5A) (calcium? or potassium?)) or ((intermediate
conductance) (5A) "Ca2+") or "IKCa" or "KCa"
          3431 ((INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?)) OR
1.27
               ((INTERMEDIATE CONDUCTANCE) (5A) "CA2+") OR "IKCA" OR "KCA"
=> s 118 or 121 or 127
         4411 L18 OR L21 OR L27
L28
=> s 124 and 128
           32 L24 AND L28
L29
=> dup rem
ENTER L# LIST OR (END):129
PROCESSING COMPLETED FOR L29
             20 DUP REM L29 (12 DUPLICATES REMOVED)
L30
                ANSWERS '1-8' FROM FILE MEDLINE
                ANSWERS '9-12' FROM FILE BIOSIS
                ANSWERS '13-18' FROM FILE CAPLUS
                ANSWER '19' FROM FILE EMBASE
                ANSWER '20' FROM FILE WPIDS
=> d 130 1-20 ibib ed abs
L30 ANSWER 1 OF 20
                                                         DUPLICATE 1
                        MEDLINE on STN
ACCESSION NUMBER:
                    2004296482
                                MEDLINE
                    PubMed ID: 15127180
DOCUMENT NUMBER:
TITLE:
                    Small and intermediate conductance Ca(2+)-activated K+
                    channels confer distinctive patterns of distribution in
                    human tissues and differential cellular localisation in the
                    colon and corpus cavernosum.
                    Chen Mao Xiang; Gorman Shelby A; Benson Bill; Singh Kuljit;
AUTHOR:
                    Hieble J Paul; Michel Martin C; Tate Simon N; Trezise Derek
```

Gene Expression and Protein Biochemistry, GlaxoSmithKline

CORPORATE SOURCE:

R32-R34=H, 1-10C halo upto perhaloalkyl, 1-10C alkyl, 3-12C cycloalkyl, 2-10C alkenyl, 5-7C cycloalkenyl or 3-10C alkynyl, or CR34=3-6C spiro ring, or

R34 + adjacent C atom to which it is attached = fused ring containing 3-7 and 4-14H atoms, or

R34 + C atom 2-4C atoms from attached C atom = fused ring containing 3-7 and 4-14H atoms;

R35 = 6-12C aryl or heteroaryl having 2-11C atoms and 1-3 N, S and O heteroatoms;

R36 = 6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O heteroatoms, 1-10C alkyl, 3-12C cycloalkyl, heterocyclylalkyl having 4-7C and 1-3 N, S and O heteroatoms, 2-10C alkenyl, 5-12C cycloalkenyl or R17-R18.

The proviso for T in (IV) does not apply.

ACTIVITY - Osteopathic; Contraceptive; Gynecological; Tocolytic; Analgesic; Nootropic; Antidepressant; Cardiant; Cytostatic; Depilatory. MECHANISM OF ACTION - Progesterone receptor (PR) modulator.

In a PR receptor binding assay for measuring inhibition of binding of tritiated progesterone to PR in T47D cell cytosol, N-(4-(2-ethylbutyl)-4-azatricyclo(4,3,1,138)undec-5-ylidene) -2-methyl-4-nitroaniline (Ia) inhibited 80-100% binding at 200 nM.

USE - Used for enhancing bone formation in bone weakening diseases for treating osteopenia or osteoporosis, fracture healing, recognition and maintenance of pregnancy, sensory and motor functions, short term memory and male and female sexual receptivity, preventing endometrial implantation, postsurgical adhesion formation and myocardial infarction, inducing labor, treating luteal deficiency, preecamplsia, eclampsia of pregnancy, preterm labor, infertility, dysmenorrhea, dysfunctional uterine bleeding, ovarian hyperandrogynism, ovarian hyperaldosteronism, premenstrual syndrome and tension, premenstrual behavior disorders, climeracteric disturbance, post menopausal urinary incontinence, postpartum depression, genital atrophy, cancers, endometriosis, uterine fibroids, hirsutism and hair growth, use as a female contragestive agent, regulating uterine immune function, hormone replacement, male contraception, abortion and promoting mylin repair

ADVANTAGE - The compounds have fewer side effects. $\ensuremath{\mathsf{Dwg.0/0}}$

=> d his

(FILE 'HOME' ENTERED AT 12:07:55 ON 14 APR 2005)

FILE 'CAPLUS' ENTERED AT 12:08:10 ON 14 APR 2005 ACTIVATE L09939093/L

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L1
L2
             50) SEA FILE=REGISTRY SSS SAM L1
L3
              0) SEA FILE=REGISTRY EXA FUL L1
1.4
           4907) SEA FILE=REGISTRY SSS FUL L1
L5
             61) SEA FILE=CAPLUS ABB=ON
                                         PLU=ON
L6
            112) SEA FILE=CAPLUS ABB=ON
                                         PLU=ON
                                                 L2 OR "1-ETHYL-2-BENZIMIDAZOLIN
L7
              1) SEA FILE=CAPLUS ABB=ON
                                         PLU=ON
                                                 L6 AND (SEXUAL DYSFUNCTION? OR
L8
              0) SEA FILE=CAPLUS ABB=ON
                                         PLU=ON
                                                 L6 AND GENITALIA?
L9
              1) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                                 L6 AND (SEXUAL?)
L10
                STR
L11 (
             50) SEA FILE=REGISTRY SSS SAM L10
L12 (
           4907) SEA FILE=REGISTRY SSS FUL L1
L13 (
          13889) SEA FILE=REGISTRY SSS FUL L10
L14 (
             58) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                 L13 AND (SEXUAL DYSFUNCTION? OR
L15 (
              1) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                                 L14 AND (CALCIUM CHANNEL?)
L16 (
              5) SEA FILE=CAPLUS ABB=ON
                                        PLU=ON
                                                 L14 AND CALCIUM?
L17 (
             53) SEA FILE=CAPLUS ABB=ON PLU=ON L14 NOT (L15 OR L16)
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R8 = H, halo or 1-4C alkyl;
y = 0-2;
     g = 0-4, except where G is halo which may be present to perhalo
level;
     X = 3-7C alkyl or 3-7C alkenyl, or
     X = a group forming a polycyclic 3-4 ring structure, each ring of
3-8C and optionally substituted by at least one 1-6C alkyl or 2-6C
alkenyl;
     R10-R12 = H, 1-10C halo upto perhaloalkyl, 1-10C alkyl, 3-12C
cycloalkyl, 2-10C alkenyl, 5-7C cycloalkenyl or 3-10C alkynyl, or CR12 = 3-6C spiro ring, 3-7C and 4-14H fused ring or
     R12 + the C atom 2-4C atoms from the attached C atom = a 3-7C and
4-14H fused ring;
     R13 = 6-12C aryl or 4-pyridyl;
     R14 = 6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O
heteroatoms, 1-10C alkyl, 3-12C cycloalkyl, heterocyclylalkyl having 4-7C
and 1-3 N, S and O heteroatoms, 2-10C alkenyl, 5-12C monocycloalkenyl or
R17-R18;
     R17 = 1-10C alkyl or 2-10C alkenyl;
     R18 = 6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O
heteroatoms, 3-12C cycloalkyl, heterocyclylalkyl having 4-7C and 1-3 N, S
and O heteroatoms or 5-12C cycloalkenyl;
     R15, R16 = H, 6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O
heteroatoms, 1-10C alkyl, 3-12C cycloalkyl, heterocycloalkyl having 4-7C and 1-3 N, S and O heteroatoms, 2-10C alkenyl, 5-12C cycloalkenyl or
R19-R20, so that the total number of non H atoms on R14-R16 is at least 9,
     NR15R16 = 5-8 membered ring containing 4-7C and 1 or 2 N, S and O
heteroatoms (optionally substituted by R21 and R22);
     R19 = 1-10C alkyl, 3-12C cycloalkyl, heterocycloalkyl having 4-7C and
1-3 N, S and O heteroatoms, 2-10C alkenyl or 5-12C cycloalkenyl;
     R20 = H, 6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O
heteroatoms, 3-12C cycloalkyl, heterocycloalkyl having 4-7C and 1-3 N, S
and O heteroatoms, 5-12C cycloalkenyl or R23-R24;
     R23 = 6-12C aryl, heteroaryl having 2-11C and 1-3 N, S and O
heteroatoms;
     R24 = H, halo, CN, NO2, 1-10C alkyl, 1-6C haloalkyl having 1-3 halo;
     R21, R22 = H, 1-10C halo upto perhaloalkyl, 1-10C alkyl, 6-12C aryl,
heteroaryl having 2-11C and 1-3 N, S and O heteroatoms or
benzimidazolinone, or
     CR21 or CR22 = fused ring having 3-6C and 4-10H atoms, or
     R22 + adjacent C to which it is attached = fused ring having 3-6C and
4-10H atoms;
provided that:
     (i) when X is 3-4C alkyl and R10-R12 are H; t is 1; at least one T is
4-NO2 or 4-CN and at least one other T is 2-alkyl, 2-halo or 2-CF3, and R1
is phenyl;
     (ii) when X is 3-7C alkyl or 3-7C alkenyl and R10-R12 are H, 1-10C
halo upto perhaloalkyl, 1-10C alkyl, 3-12C cycloalkyl, 2-10C alkenyl, 5-7C
cycloalkenyl or 3-10C alkynyl, then at least one T is NO2, CN, CF3 or
halo;
     (iii) when R13 is 6-12C aryl, at least one T is NO2, CN, CF3 or halo;
     (iv) in (II), when NR15R16 form morpholine, the morpholine is
substituted by R21 and/or R22, and
     (v) when R20 is phenyl, one of R15 a R16 is R19-R20.
     An INDEPENDENT CLAIM is included for treating diseases or conditions
(see 'USE' section) which comprises administering a compound of formula
(III) or (IV).
     R26 = H, 1-10C alkyl, 1-10C halo upto perhaloalkyl, 3-12C
cycloalkyl, heterocycloalkyl with 4-7C and 1-3 N, S and O heteroatoms,
2-10C alkenyl, 5-12C mono- to tri-cyclic cycloalkenyl, or 3-10C alkynyl;
     X' = a group of formula (i);
n = 3-7;
p = 0-7;
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BR 2001007179
               A 20020702 (200252)
               A 20030205 (200334)
CN 1395467
EP 1317456
               A2 20030611 (200339)
                                     EN
    R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT
       RO SE SI TR
ZA 2002003389
               A 20030625 (200348)
                                          143
US 2003229072
               A1 20031211 (200382)
JP 2004508373
               W 20040318 (200420)
                                         225
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APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2002020526	A2	WO 2001-US27007	20010830
AU 2001088529	A	AU 2001-88529	20010830
BR 2001007179	A	BR 2001-7179	20010830
		WO 2001-US27007	20010830
CN 1395467	A	CN 2001-803536	20010830
EP 1317456	A2	EP 2001-968272	20010830
		WO 2001-US27007	20010830
ZA 2002003389	A	ZA 2002-3389	20020429
US 2003229072	A1	WO 2001-US27007	20010830
		US 2003-363621	20030303
JP 2004508373	W	WO 2001-US27007	20010830
		JP 2002-525147	20010830

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2001088529	A Based on	WO 2002020526
BR 2001007179	A Based on	WO 2002020526
EP 1317456	A2 Based on	WO 2002020526
JP 2004508373	W Based on	WO 2002020526

PRIORITY APPLN. INFO: US 2000-656854 20000907

ED 20020704

AN 2002-393837 [42] WPIDS

AB WO 200220526 A UPAB: 20030317

NOVELTY - Cyclic and acyclic amidine compounds (I) and (II) are new.

DETAILED DESCRIPTION - Cyclic amidine compounds of formula (I) and acyclic amidine compounds of formula (II) and their salts, are new.

R1 = 6-12C aryl or heteroaryl with 2-11 carbon and 1-3 N, O or S heteroatoms;

T = H, NO2, CN, 1-6C alkyl, 1-6C halo upto perhaloalkyl, 6-12C aryl or heteroaryl with 2-11 carbon and 1-3 N, O or S heteroatoms, or

T + adjacent C atom = a fused ring of 6-9 C and 4-14 hydrogen atoms; t = 1-5;

R2 = 2-10C alkyl, 1-10C halo upto perhaloalkyl, 3-12C cycloalkyl, heterocycloalkyl with 4-7C and 1-3 N, S and O heteroatoms, 2-10C alkenyl, 5-12C mono- to tri-cyclic cycloalkenyl, or 3-10C alkynyl;

G = H, NO2, CN, halo, OH, OR4, oxo, 1-4C halo upto perhaloalkyl, or 1-4C alkyl, 2-4C alkenyl, 3-7C cycloalkyl, heterocycloalkyl of 3-5 C and 1-3 N, O and S heteroatoms, 5-7C cycloalkenyl or heterocycloalkenyl of 4-6C and 1-3 N, O and S heteroatoms (all optionally substituted by at least 1 halo upto perhalo), COOR4, CONR5R6, or 6-10C aryl or heteroaryl of 3-9C and 1-3 N, O and S heteroatoms (both optionally substituted by 1-3 alkyl and halo upto perhalo), S(O)yR7, SO3R7 or SO2NR5R6;

R4 = 1-4C alkyl, 1-4C halo upto perhaloalkyl, 3-6C cycloalkyl or 3-6C halocycloalkyl;

R5, R6 = H or 1-5C alkyl;

R7 = 1-5C alkyl, fluorosulfonyl, formyl, OH, CN, halo, N-oxide, OC(R8)2O, CONHCO (with C atoms attached to adjacent positions on R) or CO-phenyl, attached to R ortho to the carbonyl;

an amount as to cause MED and has a direct effect on the endogenous erectile process in the corpus cavernosum of the male;

- (6) A diagnostic composition or kit comprising (A);
- (7) An animal model for identifying an agent capable of treating MED comprising:
 - (a) an anaesthetized animal; and
- (b) the means to measure changes in intracavernosal pressure and/or cavernosal blood flow of animal following stimulation of the pelvic nerve;
- (8) An assay method (M5) involves administering an agent to the animal model and measuring the change in the endogenous erectile process; and
- (9) A combination containing at least one NPYi and at least one auxiliary active agents (e.g. PDE inhibitor) in the manufacture/preparation of a medicament for the treatment or prevention of MED.

ACTIVITY - Vasotropic; Anorectic.

Submaximal increases in intracavernosal pressure (ICP) induced by nerve stimulation were significantly increased in the presence of increasing doses of ((2-diphenylacetylamino-5-guanidino-pentanoyl)-4-hydroxy-benzylamide), a selective NPY Y1 receptor antagonist.

The increase became significant at doses at least 30 micro g/kg. The maximum potentiation (approximately 127%) was observed at 30 micro g/kg.

MECHANISM OF ACTION - Neuropeptide Y (NPY) inhibitor; NPY receptor antagonist.

USE - For treatment or prevention of male **erectile dysfunction**, abnormal drink and food intake disorders (e.g. obesity, anorexia, bulimia or metabolic disorders) (claimed).

ADVANTAGE - The inhibitor has no activity towards endopeptidase (NEP) and/or angiotensin converting enzyme; selectively increases intracavernosal pressure of the penis which facilitates and/or causes penile erection during sexual arousal; is highly selective for NPY/NPY Y1 located in male genitalia and for NPY and/or NPY Y1 receptors associated with the corpus cavernosum. The NPY inhibitors enhance the nerve-stimulated erectile process and are highly selective for reproductive tract to overcome an erectile dysfunction without the risk of adverse side effects, particularly a drop in blood pressure. Dwg.0/10

L26 ANSWER 6 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN

ACCESSION NUMBER:

2002-393837 [42] WPIDS

DOC. NO. CPI:

C2002-110754

TITLE:

New cyclic and acyclic amidine derivatives are progesterone receptor modulators used for treating osteoporosis and for fertility control.

DERWENT CLASS:

B02

INVENTOR(S):

BULLOCK, W H; COLLIBEE, W L; DALLY, R; KLUENDER, H C E;

RODRIGUEZ, M E; WANG, M; RODRIQUEZ, M E

PATENT ASSIGNEE(S):

(FARB) BAYER CORP; (BULL-I) BULLOCK W H; (COLL-I)

COLLIBEE W L; (DALL-I) DALLY R; (KLUE-I) KLUENDER H C E;

(RODR-I) RODRIGUEZ M E; (WANG-I) WANG M

COUNTRY COUNT: 9

PATENT INFORMATION:

PATENT NO KIND DATE WEEK LA PG

WO 2002020526 A2 20020314 (200242)* EN 132

RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PH PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW

AU 2001088529 A 20020322 (200251)

			US	2001-17273	20011212
EΡ	1347750	A1	ΕP	2001-270206	20011210
		•	WO	2001-IB2399	20011210
KR	2003061441	A	KR	2003-707946	20030613
CN	1496254	A	CN	2001-820556	20011210
HU	2004000528	A2	WO	2001-IB2399	20011210
			HU	2004-528	20011210
JP	2004522720	W	WO	2001-IB2399	20011210
			JΡ	2002-549244	20011210
WT	220650	B1	TW	2001-128451	20011116
ΝZ	526925	A	ΝZ	2001-526925	20011210
			WO	2001-IB2399	20011210

FILING DETAILS:

	PATENT NO	KIND	PATENT NO	•
	AU 2002020977 EP 1347750	Al Based on	WO 200204767	0
	HU 2004000528			· *
	JP 2004522720			-
	NZ 526925	A Based on	WO 200204767	0 .
PRIO	RITY APPLN. INFO			
		2000-30647	20001215; GB	
		2001-8730	20010406; GB	•
		2001-9910	20010423; GB	•
		2001-11037	20010504; US	
		2001-895367	20010629; US	
		2001-905846	20010713; US	
		2001-948429	20010907; WO	
	•	2000-GB4380	20001117	
ED	20020910			
AN	2002-547828 [58] WPIDS		
CR	2002-155042 [20]; 2002-179661	[23]; 2002-241363	[29]; 2002-740638 [8
AB	WO 200247670 A			

NOVELTY - Use of an inhibitor (NPYi) of a neuropeptide Y (NPY) for the treatment or prevention of male erectile dysfunction (MED).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

- (1) Use a neuropeptide Y Y1 receptor (NP Y1) inhibitor (NP Y1i) for the treatment or prevention of male erectile dysfunction (MED);
- (2) An assay method (M1) for identifying an agent that can be used to treat to MED comprising:
- (a) determining whether the test agent (A) (such as NPYi) directly enhances the endogenous erectile process;
 - (3) A process (M2) involving:
 - (a) performing (M1);
- (b) identifying at least one agent capable of inhibiting NPY or NPY
- (c) preparing a quantity of those identified agents (NPYi or NPY Y1i);
 - (4) An assay method (M3) comprising:
- (a) contacting (A) which has a moiety capable of inhibiting the metabolic breakdown of a peptide (preferably a fluorescent labeled peptide); and
- (b) measuring the activity and/or levels of peptide remaining after a fixed time (e.g. via fluorometric analysis. Where the change in the level of the peptide measured by fluorescence is indicative of the potency of (A);
 - (5) A diagnostic method (M4) involves:
 - (a) isolating a sample from a male; and
 - (b) determining whether the sample contains an entity present in such

2002-155042 [20]; 2002-179661 [23]; 2002-241363 [29]; CROSS REFERENCE: 2002-740638 [80] DOC. NO. CPI: C2002-155371 TITLE: Use of an inhibitor of neuropeptide Y in the preparation of medicament for the treatment or prevention of male erectile dysfunction. DERWENT CLASS: INVENTOR(S): BENSON, N; BOYD, H F; CONTILLO, L G; SINGLETON, D H; STACEY, P; NAYLOR, A M; VAN DER GRAAF, P H; WAYMAN, C P; GONZALEZ, M I; HIGGINBOTTOM, M; PINNOCK, R D; PRITCHARD, M C; STOCK, H T PATENT ASSIGNEE(S): (NAYL-I) NAYLOR A M; (PFIZ) PFIZER INC; (PFIZ) PFIZER LTD; (WARN) WARNER LAMBERT CO; (GONZ-I) GONZALEZ M I; (HIGG-I) HIGGINBOTTOM M; (PINN-I) PINNOCK R D; (PRIT-I) PRITCHARD M C; (STOC-I) STOCK H T; (VGRA-I) VAN DER GRAAF P H; (WAYM-I) WAYMAN C P COUNTRY COUNT: 102 PATENT INFORMATION: WEEK LA PG PATENT NO KIND DATE ______ WO 2002047670 A1 20020620 (200258)* EN 179 RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TR TZ UG ZM ZW W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SD SE SG SI SK SL TJ TM TN TR TT TZ UA UG US UZ VN YU ZA ZW A 20020624 (200267) AU 2002020977 A1 20021114 (200277) US 2002169101 A2 20030115 (200306) EP 1275733 ΕN R: AL AT BE BG CH CY CZ DE DK EE ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI SK TR A1 20030113 (200313) CA 2393376 EN A 20030513 (200340) JP 2003135064 92 US 2003119714 A1 20030626 (200343) A1 20031001 (200365) EN EP 1347750 R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI TR KR 2003061441 A 20030718 (200381) A 20040512 (200452) CN 1496254 HU 2004000528 A2 20040628 (200452) JP 2004522720 W 20040729 (200452) 275 TW 220650 B1 20040901 (200522) NZ 526925 A 20050324 (200523) APPLICATION DETAILS: PATENT NO APPLICATION KTND DATE WO 2001-IB2399 20011210 All 2002-20977 20011210 WO 2002047670 A1 AU 2002020977 A AU 2002-20977
US 2002169101 Al Provisional US 1999-133355P
CIP of WO 2000-GB1787
CIP of US 2000-700165
CIP of US 2001-759777 20011210 19990510 20000510 20001109 20010112 US 2001-999284 -20011115 EP 2002-254616 EP 1275733 EP 2002-203011 CA 2002-2393376 Α2 20020701 CA 2393376 A1 20020711 Al Provisional US 2001-265358P
Provisional US 2001-291722P
CIP of US 2001-895367
US 2001-905846 JP 2003135064 20020715 US 2003119714 20010131

20010517 20010629

20010713

US 2001-905846

for ATP-sensitive K+ channels, Ca2+-activated K+ channels and voltage-dependent K+ channel-KQT-like subfamily (KCNQ) members, and has paved the way in the assessment of efficacy and adverse effects in preclin. models. This review focuses on the rationale for mol. targeting of K+ channels, the current status of target validation, including preclin. proof-of-concept studies, and provides perspectives on the limitations and hurdles to be overcome in realizing the potential of these targets for diverse urol. indications such as overactive bladder, erectile dysfunction and prostate diseases.

REFERENCE COUNT:

216 THERE ARE 216 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE REFORMAT

L26 ANSWER 4 OF 6 EMBASE COPYRIGHT 2005 ELSEVIER INC. ALL RIGHTS RESERVED.

on STN

ACCESSION NUMBER: 20041

2004123250 EMBASE

TITLE:

EDHF: New therapeutic targets?.

AUTHOR:

Feletou M.; Vanhoutte P.M.

CORPORATE SOURCE:

M. Feletou, Dept. Diabete Maladies Metaboliques, Institut

de Recherches Servier, 11 rue des Moulineau, 92150 Suresnes, France. michel.feletou@fr.netgrs.com

SOURCE:

Pharmacological Research, (2004) Vol. 49, No. 6, pp.

565-580.

Refs: 244

ISSN: 1043-6618 CODEN: PHMREP

PUBLISHER IDENT.:

S 1043-6618(03)00411-0

COUNTRY:

United Kingdom

DOCUMENT TYPE:

Journal; General Review

FILE SEGMENT:

005 General Pathology and Pathological Anatomy

030 Pharmacology

037 Drug Literature Index

LANGUAGE:

English

SUMMARY LANGUAGE: ENTRY DATE:

English
Entered STN: 20040412

Last Updated on STN: 20040412

ED Entered STN: 20040412

Last Updated on STN: 20040412

AB Besides cyclooxygenase and NO-synthase, another distinct endothelial pathway, endothelium-dependent hyperpolarization (EDHF), is involved in the relaxation of the vascular smooth muscle cells. EDHF has been demonstrated unequivocally in various blood vessels from different species, including human, and is likely to play an important role in cardiovascular physiology. This alternative pathway involves the activation of two populations of endothelial potassium channels, the small conductance and intermediate conductance

calcium-activated potassium channels

(SK(Ca) and IK(Ca), respectively). EDHF-mediated responses are clearly altered in various pathological conditions (ageing, hypertension, atherosclerosis, hypercholesterolemia, heart failure, ischemia-reperfusion, angioplasty, eclampsia, diabetes, sepsis). Therapeutic or adjutant interventions (angiotensin converting enzyme inhibitors, antagonist of the angiotensin receptor, estrogen, omega-3 polyunsaturated fatty acids, polyphenol derivatives, potassium and/or calcium intake) can restore these responses, suggesting that the improvement of the EDHF pathway contributes to the observed beneficial effect of these various substances. However, the improvement or restoration of EDHF responses has not been, yet, the direct purpose of any pharmaceutical effort. Activating endothelial IK(Ca) and/or SK(Ca) or increasing their expression as well as improving myo-endothelial communication, for instance by increasing the expression of connexin(s), could become interesting therapeutic targets. .COPYRGT. 2004 Elsevier Ltd. All rights reserved.

L26 ANSWER 5 OF 6 WPIDS COPYRIGHT 2005 THE THOMSON CORP on STN ACCESSION NUMBER: 2002-547828 [58] WPIDS

PATENT ASSIGNEE(S):

Pfizer Limited, UK; Pfizer Inc.

SOURCE:

PCT Int. Appl., 120 pp. CODEN: PIXXD2

DOCUMENT TYPE:

Patent

English

LANGUAGE:

FAMILY ACC. NUM. COUNT:

PATENT INFORMATION:

PAT	TENT	NO.			KIN	D -	DATE			APPL	ICAT	ION I	NO.		D.	ATE	
	2002 2002						2002 2002		. 1	WO 2	001-	IB15	25		2	0010	824
	W:	CO, GM, LS, PT,	CR, HR, LT, RO,	CU, HU, LU, RU,	CZ, ID, LV, SD,	DE, IL, MA, SE,	DK, IN, MD, SG,	DM, IS, MG, SI,	DZ, JP, MK, SK,	EC, KE, MN, SL,	BG, EE, KG, MW, TJ,	ES, KP, MX, TM,	FI, KR, MZ, TR,	GB, KZ, NO, TT,	GD, LC, NZ, TZ,	GE, LK, PH, UA,	GH, LR, PL,
	RW:	GH, DE,	GM, DK,	KE, ES,	LS, FI,	MW, FR, CM,	MZ, GB, GA,	SD, GR, GN,	SL, IE, GQ,	SZ, IT, GW,	KG, TZ, LU, ML,	UG, MC, MR,	ZW, NL, NE,	AT, PT, SN,	BE, SE, TD,	CH, TR, TG	BF,
AU	2420 2001 1313	0823	77		AA A5		2002	0313		AU 2	001- 001- 001-	8237	7		2	0010	824
Er		AT,	BE,	CH,	DE,	DK,		FR,	GB,	GR,	IT,						
	2004 2004	1850	94					0923		US 2	002- 001-	9390	93		2	0010 0010 0000	824
			21.10	• •					:	US 2	000-	2382	06P]	2	0000 0001 0010	005

ED Entered STN: 08 Mar 2002

A method of treating an individual is described. The method comprise AB delivering to the individual an agent that is capable of modulating an intermediate conductance calcium-activated potassium (IKCa) channel in the sexual genitalia of the individual; wherein the modulation of the IKCa channel by the agent is capable of mediating a relaxation of corpus cavernosal smooth muscle tone. The agent may be admixed with a pharmaceutically acceptable carrier, diluent or excipient.

L26 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:

2004:816279 CAPLUS

DOCUMENT NUMBER:

142:168588

TITLE:

Potassium channel subtypes as molecular targets for overactive bladder and other urological disorders

AUTHOR(S):

Gopalakrishnan, Murali; Shieh, Char-Chang

CORPORATE SOURCE:

Neuroscience Research, Global Pharmaceutical Research and Development, Abbott Laboratories, Abbott Park, IL,

60064, USA

SOURCE:

Expert Opinion on Therapeutic Targets (2004), 8(5),

437-458

CODEN: EOTTAO; ISSN: 1472-8222

PUBLISHER:

Ashley Publications Ltd.

DOCUMENT TYPE:

Journal; General Review

LANGUAGE: English Entered STN: 07 Oct 2004

A review. Potassium channels have re-emerged as attractive targets for overactive bladder and other urol. diseases in recent years, in part due to an enhanced understanding of their mol. heterogeneity, tissue distribution, functional roles and regulation in physiol. and pathol. states. Cloning and heterologous expression anal., coupled with the advancement of improved high-throughput screening techniques, have enabled expeditious identification of selective small-mol. openers and blockers

L26 ANSWER 1 OF 6 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2004296482 MEDLINE PubMed ID: 15127180 DOCUMENT NUMBER:

Small and intermediate conductance Ca(2+)-activated K+ TITLE: channels confer distinctive patterns of distribution in

human tissues and differential cellular localisation in the

colon and corpus cavernosum.

AUTHOR: Chen Mao Xiang; Gorman Shelby A; Benson Bill; Singh Kuljit;

Hieble J Paul; Michel Martin C; Tate Simon N; Trezise Derek

Gene Expression and Protein Biochemistry, GlaxoSmithKline CORPORATE SOURCE:

R&D, Gunnels Wood Road, Stevenage, Hertfordshire, SG1 2NY,

UK.. mark.x.chen@qsk.com

Naunyn-Schmiedeberg's archives of pharmacology, (2004 Jun) SOURCE:

369 (6) 602-15. Electronic Publication: 2004-05-01.

Journal code: 0326264. ISSN: 0028-1298. PUB. COUNTRY: Germany: Germany, Federal Republic of DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200502

ENTRY DATE: Entered STN: 20040616

> Last Updated on STN: 20050223 Entered Medline: 20050222

ED Entered STN: 20040616

> Last Updated on STN: 20050223 Entered Medline: 20050222

AΒ The SK/IK family of small and intermediate conductance

calcium-activated potassium channels

contains four members, SK1, SK2, SK3 and IK1, and is important for the regulation of a variety of neuronal and non-neuronal functions. In this study we have analysed the distribution of these channels in human tissues and their cellular localisation in samples of colon and corpus cavernosum. SK1 mRNA was detected almost exclusively in neuronal tissues. SK2 mRNA distribution was restricted but more widespread than SK1, and was detected in adrenal gland, brain, prostate, bladder, liver and heart. SK3 mRNA was detected in almost every tissue examined. It was highly expressed in brain and in smooth muscle-rich tissues including the clitoris and the corpus cavernosum, and

expression in the corpus cavernosum was upregulated up to 5-fold in patients undergoing sex-change operations. IK1 mRNA was present in surface-rich, secretory and inflammatory cell-rich tissues, highest in the trachea, prostate, placenta and salivary glands. In detailed immunohistochemical studies of the colon and the corpus cavernosum, SK1-like immunoreactivity was observed in the enteric neurons. SK3-like immunoreactivity was observed strongly in smooth muscle and vascular endothelium. IK1-like immunoreactivity was mainly observed in inflammatory cells and enteric neurons of the colon, but absent in corpus cavernosum. These distinctive patterns of

distribution suggest that these channels are likely to have different biological functions and could be specifically targeted for a number of human diseases, such as irritable bowel syndrome, hypertension and erectile dysfunction.

L26 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN DUPLICATE 2

ACCESSION NUMBER: 2002:171727 CAPLUS

DOCUMENT NUMBER: 136:210533

TITLE: Intermediate conductance

calcium-activated potassium channel modulators in treatment of

erectile dysfunction

INVENTOR(S): Maw, Graham Nigel; Wayman, Christopher Peter FILE 'EMBASE' ENTERED AT 12:08:44 ON 14 APR 2005 COPYRIGHT (C) 2005 Elsevier Inc. All rights reserved.

FILE 'WPIDS' ENTERED AT 12:08:44 ON 14 APR 2005 COPYRIGHT (C) 2005 THE THOMSON CORPORATION

- => s (intermediate conductance calcium activated potassium channel?) or "IKCa" L18 487 (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANNEL?) OR "IKCA"
- => s (sexual dysfunction? or sexual disfunction? or erectile dysfunction? or erectile disfunction? or penile erect? or penile blood flow or penile circulation? or tumescen? or impoten? or corpus cavernos?
 UNMATCHED LEFT PARENTHESIS '(SEXUAL'
 The number of right parentheses in a query must be equal to the number of left parentheses.
- => s (sexual dysfunction? or sexual disfunction? or erectile dysfunction? or erectile disfunction? or penile erect? or penile blood flow or penile circulation? or tumescen? or impoten? or corpus cavernos?)
- L19 63399 (SEXUAL DYSFUNCTION? OR SEXUAL DISFUNCTION? OR ERECTILE DYSFUNCT ION? OR ERECTILE DISFUNCTION? OR PENILE ERECT? OR PENILE BLOOD FLOW OR PENILE CIRCULATION? OR TUMESCEN? OR IMPOTEN? OR CORPUS CAVERNOS?)
- => s (female sexual dysfunction? or female sexual disfunction? or female sexual
 arousal disorder? or female sexual arousal dysfunction? or female sexual arousal
 disfunction? or clitoral corpus cavernos?)
 4 FILES SEARCHED...
- L20 1658 (FEMALE SEXUAL DYSFUNCTION? OR FEMALE SEXUAL DISFUNCTION? OR FEMALE SEXUAL AROUSAL DISORDER? OR FEMALE SEXUAL AROUSAL DYSFUNCTION? OR CLITORAL CORPUS CAVERNOS?)
- => s benzimidazolinone? or "1-ethyl-2-benzimidazolinone" or "EBIO" or "1-EBIO" L21 1081 BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBIO" OR "1-EBIO"

=> s 119 or 120 L22 63430 L19 OR L20

=> s clitor? or genital? or sexual genital? or penis? or penile? or erectile tissue? L23 343217 CLITOR? OR GENITAL? OR SEXUAL GENITAL? OR PENIS? OR PENILE? OR ERECTILE TISSUE?

=> s 122 or 123 L24 381006 L22 OR L23

=> dup rem 125

PROCESSING COMPLETED FOR L25

L26 6 DUP REM L25 (4 DUPLICATES REMOVED)
ANSWER '1' FROM FILE MEDLINE
ANSWERS '2-3' FROM FILE CAPLUS
ANSWER '4' FROM FILE EMBASE
ANSWERS '5-6' FROM FILE WPIDS

=> s 126 1-6 ibib ed abs
MISSING OPERATOR L26 1-6
The search profile that was entered contains terms or
nested terms that are not separated by a logical operator.

=> file caplus
COST IN U.S. DOLLARS

SINCE FILE TOTAL ENTRY SESSION 0.21 0.21

FULL ESTIMATED COST

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FILE COVERS 1907 - 14 Apr 2005 VOL 142 ISS 16 FILE LAST UPDATED: 13 Apr 2005 (20050413/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

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L1
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L2
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L3
              0) SEA FILE=REGISTRY EXA FUL L1
L4
           4907) SEA FILE=REGISTRY SSS FUL L1
L5
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L6
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L7
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L9
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L10
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L15 (
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L16 (
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                                                 L14 AND CALCIUM?
L17 (
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FILE 'MEDLINE' ENTERED AT 12:08:44 ON 14 APR 2005

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S23	346	(calcium adj activated adj potassium)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 17:16
S24	76	S23 and sexual\$	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 17:16
S25	28	("5767139" "5696146" "5912357" "6514975" "6440982" "6756373" "6503908" "6734186" "6831074" "6593332" "6586439" "5922747" "6200978" "6262046" "6333330"). pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR .	OFF	2005/04/13 12:42
S26	3	("6734186" "6878529").pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR ·	OFF	2005/04/13 12:42
S27	346	(calcium adj activated adj potassium)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/14 11:55
S28	200	(calcium adj activated adj potassium) and (smooth adj muscle)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/13 16:22
S29	22	(intermediate adj conductance adj calcium adj activated adj potassium) and (smooth adj muscle)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/13 16:13
S30	52	(intermediate adj conductance) near5 potassium	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/13 16:22

S13	1	S12 and calcium	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 16:49
S14	0	S12 and channel	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 16:49
S15	2	wo-9534555-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 16:50
S16	2	ep-477819-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 16:50
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S19	1	de-2801868-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 17:13
S20	5	("4420486" "4133958").pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 17:14
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S22	. 1	gb-1564182-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/14 11:15

S3	341	S1 not S2	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 15:33
S4	5774	(calcium adj channel adj blocker\$)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 15:33
S5	397	S4 and ((sexual adj dysfunction) or (sexual adj disfunction) or (erectile adj dysfunction) or (male adj sexual adj dysfunction) or (female adj sexual adj dysfunction))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 15:35
S6	397	S5 not S3	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 16:39
S7	2	"5770606".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 16:41
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S9	2	wo-9831368-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 16:45
S10	2	wo-9728157-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 16:45
S11	2	wo-9724334-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/14 12:46
S12	2	"6166219".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 17:33

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Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
L1		"4004016".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/14 11:10
L2	2	ep-477819-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/14 11:10
L3	2	ep-598962-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/14 11:16
L4	2	"5360809".pn.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/14 11:46
L5	1	1999WO-DK00681.ap,prai.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/14 11:47
L6	349	(calcium adj activated adj potassium)	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/14 11:55
L7	1	wo-200054773-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/14 12:49
L8		wo-9831368-\$.did.	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/14 12:49
S1	364	(calcium adj channel) near5 modulat\$	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/13 11:51
S2	23	S1 and ((sexual adj dysfunction) or (sexual adj disfunction) or (erectile adj dysfunction) or (male adj sexual adj dysfunction) or (female adj sexual adj dysfunction))	US-PGPUB; USPAT; USOCR; EPO; JPO; DERWENT	OR	OFF	2005/04/12 15:34

L103 ANSWER 1 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER: 2005:76270 CAPLUS

DOCUMENT NUMBER: 142:148827

TITLE: Phosphodiesterase 5 inhibitor-5-HT1a agonist

combination for the treatment of sexual dysfunction INVENTOR(S): Naylor, Alasdair Mark; Van der Graaf, Pieter Hadewijn;

Wayman, Christopher Peter

PATENT ASSIGNEE(S): Pfizer Limited, UK; Pfizer Inc.

SOURCE: PCT Int. Appl., 62 pp.

CODEN: PIXXD2

DOCUMENT TYPE:

Patent

LANGUAGE:

English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.			KIŅD DATE			APPLICATION NO.				DATE						
WO 20	WO 2005007166			A1 20050127			WO 2004-IB2286					20040712				
W	ΑE,	AG,	AL,	AM,	ΑT,	ΑU,	ΑZ,	BA,	BB,	BG,	BR,	BW,	BY,	BZ,	CA,	CH,
	CN,	co,	CR,	CU,	CZ,	DE,	DK,	DM,	DZ,	EC,	EE,	EG,	ES,	FI,	GB,	GD,
	GE,	GH,	GM,	HR,	HU,	ID,	IL,	IN,	IS,	JP,	ΚE,	KG,	KP,	KR,	KZ,	LC,
	LK,	LR,	LS,	LT,	LU,	LV,	MA,	MD,	MG,	MK,	MN,	MW,	MX,	MZ,	NA,	NI,
	NO,	NZ,	OM,	PG,	PH,	PL,	PT,	RO,	RU,	SC,	SD,	SE,	SG,	SK,	SL,	SY,
	ТJ,	TM,	TN,	TR,	TT,	ΤZ,	UA,	UG,	US,	UZ,	VC,	VN,	YU,	ZA,	ZM,	ZW
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US 20	US 2005065158			A1		2005	0324	!	US 2	004-	8836	22		2	0040	701
PRIORITY APPLN. INFO.:						GB 2003-16673				A 20030716						
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								4	GB 2	003-	2130	8	1	A 2	0030	911
								1	US 2	003-	5120	30P		P 2	0031	017
									US 2	003~	5131	25P		P 2	0031	021

ΕD Entered STN: 28 Jan 2005

The invention discloses the use of cyclic guanosine 3', 5'-monophosphate AΒ phosphodiesterase type 5 (PDE5) inhibitors in combination with 5-HT1a agonists for the treatment of sexual dysfunction, particularly female sexual arousal disorder (FSAD) with concomitant

hypoactive sexual desire disorder (HSDD).

REFERENCE COUNT: THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L103 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2005 ACS on STN

2003:334908 CAPLUS ACCESSION NUMBER:

DOCUMENT NUMBER: 138:331715

TITLE: Use of flibanserin in the treatment of sexual

disorders

INVENTOR(S): Evans, Kenneth Robert; Borsini, Franco PATENT ASSIGNEE(S): Boehringer Ingelheim Pharma K.-G., Germany

SOURCE: PCT Int. Appl., 11 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

PATENT NO.		KIND	DATE	APPLICATION NO.	DATE
WO 200303507	12	A1	20030501	WO 2002-EP11103	20021004
W: AE,	AG, AL,	AM, AT	r, AU, AZ,	BA, BB, BG, BR, BY, BZ,	CA, CH, CN,
CO,	CR, CU,	CZ, DE	E, DK, DM,	DZ, EC, EE, ES, FI, GB,	GD, GE, GH,

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GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
                 LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
                 PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT. TZ.
                 UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
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      EP 1446122
                                 A1 20040818 EP 2002-801880
                                                                                         20021004
           R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, GZ, EE, SK
      BR 2002013358
                                 Α
                                        20041026
                                                       BR 2002-13358
                                                                                         20021004
      JP 2005506370
                                  Т2
                                          20050303
                                                          JP 2003-537639
                                                                                         20021004
      US 2003104980
                                  A1
                                          20030605
                                                          US 2002-272603
                                                                                         20021016
PRIORITY APPLN. INFO.:
                                                          EP 2001-125020
                                                                                    A 20011020
                                                          US 2001-348911P
                                                                                    P 20011023
                                                          WO 2002-EP11103
                                                                                    W 20021004
```

ED Entered STN: 02 May 2003

AB The invention discloses the use of flibanserin for the preparation of a medicament for the treatment of disorders of **sexual**

desire. Pharmaceutical formulations containing flibanserin hydrochloride are included.

REFERENCE COUNT:

THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

SINCE FILE	TOTAL
ENTRY	SESSION
22.76	185.65
SINCE FILE	TOTAL
ENTRY	SESSION
-1.46	-1.46
	ENTRY 22.76 SINCE FILE ENTRY

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=> s (nicorandil? or pinacidil? or cromakalim? or minoxidil? or aprilkalim? or loprazolam?)

L104 21870 (NICORANDIL? OR PINACIDIL? OR CROMAKALIM? OR MINOXIDIL? OR APRIL KALIM? OR LOPRAZOLAM?)

=> s 1104 and (intermediate conductance or "IKCa" or "IKCa(2+)" UNMATCHED LEFT PARENTHESIS 'AND (INTERMEDIA' The number of right parentheses in a query must be equal to the number of left parentheses.

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PROCESSING COMPLETED FOR L105

L106 5 DUP REM L105 (11 DUPLICATES REMOVED)

ANSWERS '1-5' FROM FILE MEDLINE

=> d 1106 1-5 ibib ed abs

L106 ANSWER 1 OF 5 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2003432829 MEDLINE DOCUMENT NUMBER: PubMed ID: 12934053

TITLE: Molecular basis and characteristics of KATP channel in

human corporal smooth muscle cells.

AUTHOR: Insuk S O; Chae M R; Choi J W; Yang D K; Sim J H; Lee S W

CORPORATE SOURCE: Department of Physiology and Biophysics, Seoul National

University College of Medicine, Seoul, Korea.

SOURCE: International journal of impotence research : official

journal of the International Society for Impotence

Research, (2003 Aug) 15 (4) 258-66. Journal code: 9007383. ISSN: 0955-9930.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200310

ENTRY DATE: Entered STN: 20030917

Last Updated on STN: 20031024 Entered Medline: 20031023

ED Entered STN: 20030917

Last Updated on STN: 20031024 Entered Medline: 20031023

Relaxation of the corpus cavernosum smooth muscle is an absolute prerequisite for penile erection. Potassium channels play a role in the physiologic regulation of corporal smooth muscle tone. In spite of the physiological importance of K(ATP) channel in the modulation of corporal smooth muscle tone, there is a shortage of information available about the K(ATP) channel subtype(s) present in the corporal smooth muscle. The purpose of this study was to investigate the subunit type of K(ATP) channel, that is, the combinations of the Kir subunit and the SUR subunit in the human corporal smooth muscle and determine whether the electrophysiological kinetics and pharmacological properties of K(ATP) channels meet the subunit characteristics of the ion channel. We used cultured human corporal smooth muscle cells. To determine the presence of Kir and SURs subunits, RT-PCR was performed using Kir6.1, Kir6.2, SUR1, SUR2A, and SUR2B gene-specific primers. For electrophysiological recordings, the whole-cell, inside-out, and cell-attached configurations of the patch-clamp technique were used. We observed transcripts for Kir6.1, Kir6.2, and SUR2B in mRNA isolated from smooth muscle cells of cultured human corpus carvernosum. We recorded the unitary K(ATP) channel under the condition of intracellular and extracellular 140 mM [K(+)], and the slope conductance of the channel was 42.0+/-2.6 pS which is an intermediate conductance between that of either Kir6.1 or Kir6.2. The pinacidil (10 microM) increased the magnitude of the outward K(+) current (214.6+/-89.2%, n=12, < or = 0.05), which was blocked by the subsequent addition of the specific K(ATP) channel subtype selective blocker, glibenclamide (10 microM). The SIN-1(200 microM) induced increases in whole-cell outward K(+) currents (126.0+/-1.4%, n=4). The increased currents by SIN-1 were inhibited by glibenclamide (10 microM). We are the first to show that K(ATP) channel in human corporal smooth muscle is composed of Kir6.1-Kir6.2 construct expressed with SUR2B by RT-PCR. These findings, taken together with the electrophysiological results, suggest that K(ATP) channel in corporal smooth muscle cells is composed of heteromultimers of Kir6.1 and Kir6.2 with the ratio of 3 : 1 or 4 : 0 and SUR2B.

L106 ANSWER 2 OF 5 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 1998260329 MEDLINE

DOCUMENT NUMBER: PubMed ID: 9580610

TITLE: NO-independent vasodilation to acetylcholine in the rat

isolated kidney utilizes a charybdotoxin-sensitive,

intermediate-conductance Ca(++)-activated

K+ channel.

AUTHOR: Mieyal P; Fulton D; McGiff J C; Quilley J

CORPORATE SOURCE: Department of Pharmacology, New York Medical College,

Valhalla, USA.

CONTRACT NUMBER: HL 25394 (NHLBI)

HL 49275 (NHLBI)

SOURCE:

Journal of pharmacology and experimental therapeutics,

(1998 May) 285 (2) 659-64.

Journal code: 0376362. ISSN: 0022-3565.

PUB. COUNTRY:

United States

DOCUMENT TYPE:

Journal; Article; (JOURNAL ARTICLE)

LANGUAGE:

English

FILE SEGMENT:

Priority Journals

ENTRY MONTH:

199806

ENTRY DATE:

Entered STN: 19980618

Last Updated on STN: 19980618

Entered Medline: 19980608

> Last Updated on STN: 19980618 Entered Medline: 19980608

The role of K+ channels in the nitric oxide-independent renal vasodilator AB effect of acetylcholine (Ach) was examined to address the hypothesis that the mechanism underlying this response was different from that of bradykinin, because an earlier study indicated the possibility of different mediators. We used the rat isolated, perfused kidney that was constricted with phenylephrine and treated with nitroarginine and indomethacin to inhibit nitric oxide synthase and cyclooxygenase, respectively. The nonspecific K+ channel inhibitors, procaine and tetraethylammonium (TEA), reduced vasodilator responses to Ach and cromakalim, but not those to nitroprusside. Glibenclamide, an inhibitor of ATP-sensitive K+ channels, reduced vasodilator responses to cromakalim but did not affect those to Ach or nitroprusside. Charybdotoxin, an inhibitor of Ca(++)-activated K+ channels, reduced vasodilator responses to Ach without affecting those to cromakalim or nitroprusside. Iberiotoxin and apamin, inhibitors of large- and small-conductance Ca(++)-activated K+ channels, respectively, did not reduce vasodilation induced by Ach, cromakalim or nitroprusside. The inhibitor of cytochrome P450, clotrimazole, reduced the renal vasodilator effects of Ach and bradykinin but not those of nitroprusside or SCA 40, an agonist for Ca(++)-activated K+ channels. These results suggest that in the rat kidney, Ach, like bradykinin, utilizes a charybdotoxin-sensitive Ca(++)-activated K+ channel of intermediate conductance to elicit vasodilation and that this effect may be dependent on cytochrome P450 activity.

L106 ANSWER 3 OF 5 MEDLINE on STN DUPLICATE 3

ACCESSION NUMBER: 96428976 MEDLINE DOCUMENT NUMBER: PubMed ID: 8832078

TITLE:

Contribution of calcium-activated potassium channels to the vasodilator effect of bradykinin in the isolated, perfused

kidney of the rat.

AUTHOR: CORPORATE SOURCE:

Rapacon M; Mieyal P; McGiff J C; Fulton D; Quilley J Department of Pharmacology, New York Medical College,

Valhalla 10595, USA.

CONTRACT NUMBER:

5RO1-HL-25394 (NHLBI)

SOURCE:

British journal of pharmacology, (1996 Jul) 118 (6) 1504-8.

Journal code: 7502536. ISSN: 0007-1188.

PUB. COUNTRY:

ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199702

ENTRY DATE: Entered STN: 19970219

Last Updated on STN: 19980206 Entered Medline: 19970206

ED Entered STN: 19970219

Last Updated on STN: 19980206 Entered Medline: 19970206

1. NO- and prostaglandin-independent, endothelium-dependent vasodilator AΒ responses to bradykinin are attributed to release of a hyperpolarizing factor. Therefore, the contribution of K+ channels to the renal vasodilator effect of bradykinin was examined in rat perfused kidneys that were preconstricted with phenylephrine and treated with NG-nitro-L-arginine (L-NOARG) and indomethacin to inhibit NO and prostaglandin synthesis. 2. The non-specific K+ channel inhibitors, TEA and TBA reduced vasodilator responses to bradykinin and cromakalim but not those to nitroprusside. 3. Glibenclamide, an inhibitor of ATP-sensitive K+ channels, blocked the vasodilator response to cromakalim without affecting responses to bradykinin. 4. Charybdotoxin, a selective inhibitor of Ca(2+)-activated K+ channels, greatly attenuated vasodilator responses to bradykinin without affecting those to cromakalim or nitroprusside. 5. Iberiotoxin and leiurotoxin, inhibitors of large and small conductance Ca(2+)-activated K+ channels, respectively, were without effect on vasodilator responses to bradykinin, cromakalim or nitroprusside. 6. These results implicate K+ channels, specifically Ca(2+)-activated K+ channels of intermediate conductance, in the renal vasodilator effect of bradykinin and, thereby, support a role for a hyperpolarizing factor.

L106 ANSWER 4 OF 5 MEDLINE on STN DUPLICATE 4

ACCESSION NUMBER: 90151829 MEDLINE DOCUMENT NUMBER: PubMed ID: 2515977

TITLE: Pharmacological modulation of 86Rb efflux from aortic

endothelial cells.

AUTHOR: Ramboer I; Boeynaems J M

CORPORATE SOURCE: Institute of Interdisciplinary Research, School of

Medicine, Free University of Brussels, Belgium.

SOURCE: European journal of pharmacology, (1989 Nov 21) 171 (2-3)

251-4.

Journal code: 1254354. ISSN: 0014-2999.

PUB. COUNTRY: Netherlands

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199003

ENTRY DATE: Entered STN: 19900601

Last Updated on STN: 19970203 Entered Medline: 19900319

ED Entered STN: 19900601

Last Updated on STN: 19970203 Entered Medline: 19900319

AB The ATP-induced efflux of 86Rb from prelabelled bovine aortic endothelial cells was inhibited by quinine (50 microM) but not by a tetraethylammonium (5 mM) or apamin (50 nM). Neither sulfonylureas nor pinacidil had a significant effect on the rate of 86Rb efflux from the endothelial cells. These data are consistent with the presence of intermediate conductance Ca2(+)-activated K+ channels in endothelial cells. ATP-dependent K+ channels, sensitive to sulfonylureas and pinacidil, could not be detected.

ACCESSION NUMBER: 2004606489 MEDLINE DOCUMENT NUMBER: PubMed ID: 15459245

TITLE: Voltage dependence of ATP-dependent K+ current in rat

cardiac myocytes is affected by IK1 and IK(ACh).
Wellner-Kienitz Marie-Cecile; Bender Kirsten; Rinne

Andreas; Pott Lutz

CORPORATE SOURCE: Department of Physiology, Ruhr-University Bochum, D-44780

Bochum, Germany.

SOURCE: Journal of physiology, (2004 Dec 1) 561 (Pt 2) 459-69.

Electronic Publication: 2004-09-30. Journal code: 0266262. ISSN: 0022-3751.

PUB. COUNTRY: England: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

AUTHOR:

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200504

ENTRY DATE: Entered STN: 20041207

Last Updated on STN: 20050409 Entered Medline: 20050408

ED Entered STN: 20041207

Last Updated on STN: 20050409 Entered Medline: 20050408

AB In this study we have investigated the voltage dependence of ATP-dependent K+ current (I(K(ATP))) in atrial and ventricular myocytes from hearts of adult rats and in CHO cells expressing Kir6.2 and SUR2A. The current-voltage relation of 2,4-dimitrophenole (DNP) -induced I(K(ATP)) in atrial myocytes and expressed current in CHO cells was linear in a voltage range between 0 and -100 mV. In ventricular myocytes, the background current-voltage relation of which is dominated by a large constitutive inward rectifier (I(K1)), the slope conductance of I(K(ATP)) was reduced at membrane potentials negative to E(K) (around -50 mV), resulting in an outwardly rectifying I-V relation. Overexpression of Kir2.1 by adenoviral gene transfer, a subunit contributing to I(K1) channels, in atrial myocytes resulted in a large I(K1)-like background current. relation of I(K(ATP)) in these cells showed a reduced slope conductance negative to E(K) similar to ventricular myocytes. In atrial myocytes with an increased background inward-rectifier current through Kir3.1/Kir3.4 channels (I(K(ACh))), irreversibly activated by intracellular loading with GTP-gamma-S, the I-V relation of I(K(ATP)) showed a reduced slope negative to E(K), as in ventricular myocytes and atrial myocytes overexpressing Kir2.1. It is concluded that the voltage dependencies of membrane currents are not only dependent on the molecular composition of the charge-carrying channel complexes but can be affected by the activity of other ion channel species. We suggest that the interference between inward I(K(ATP)) and other inward rectifier currents in cardiac myocytes reflects steady-state changes in K+ driving force due to inward K+ current.

=> d his

(FILE 'HOME' ENTERED AT 12:56:43 ON 14 APR 2005)

FILE 'CAPLUS' ENTERED AT 12:56:48 ON 14 APR 2005 ACTIVATE L09939093A/L

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L1
                STR
L2
             50) SEA FILE=REGISTRY SSS SAM L1
L3
              0) SEA FILE=REGISTRY EXA FUL L1
           4907) SEA FILE=REGISTRY SSS FUL L1
L4
L5
             61) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                L_2
L6
            112) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                L2 OR "1-ETHYL-2-BENZIMIDAZOLIN
L7
              1) SEA FILE=CAPLUS ABB=ON PLU=ON
                                                L6 AND (SEXUAL DYSFUNCTION? OR
rs
              0) SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND GENITALIA?
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L9
                1) SEA FILE=CAPLUS ABB=ON PLU=ON L6 AND (SEXUAL?)
L10
                  STR
L11 (
               50) SEA FILE=REGISTRY SSS SAM L10
L12 (
            4907) SEA FILE=REGISTRY SSS FUL L1
L13 (
           13889) SEA FILE=REGISTRY SSS FUL L10
L14 (
               58) SEA FILE=CAPLUS ABB=ON PLU=ON L13 AND (SEXUAL DYSFUNCTION? OR
L15 (
              1) SEA FILE=CAPLUS ABB=ON PLU=ON L14 AND (CALCIUM CHANNEL?)
L16 (
               5) SEA FILE=CAPLUS ABB=ON PLU=ON L14 AND CALCIUM?
L17 (
              53) SEA FILE=CAPLUS ABB=ON PLU=ON L14 NOT (L15 OR L16)
          146)SEA FILE=MEDLINE ABB=ON PLU=ON (INTERMEDIATE CONDUCTANCE CALC 154)SEA FILE=BIOSIS ABB=ON PLU=ON (INTERMEDIATE CONDUCTANCE CALCI 141)SEA FILE=CAPLUS ABB=ON PLU=ON (INTERMEDIATE CONDUCTANCE CALCI
L18 (
             146) SEA FILE=MEDLINE ABB=ON PLU=ON (INTERMEDIATE CONDUCTANCE CALC
L19 (
L20 (
            29) SEA FILE=EMBASE ABB=ON PLU=ON (INTERMEDIATE CONDUCTANCE CALCI
L21 (
L22 (
             17) SEA FILE-WPIDS ABB-ON PLU-ON (INTERMEDIATE CONDUCTANCE CALCIU
           487) SEA (INTERMEDIATE CONDUCTANCE CALCIUM ACTIVATED POTASSIUM CHANN
L23 (
L24 (
           18983) SEA FILE=MEDLINE ABB=ON PLU=ON (SEXUAL DYSFUNCTION? OR SEXUAL
           12802) SEA FILE=BIOSIS ABB=ON PLU=ON (SEXUAL DYSFUNCTION? OR SEXUAL
L25 (
L26 (
           4743)SEA FILE=CAPLUS ABB=ON PLU=ON (SEXUAL DYSFUNCTION? OR SEXUAL
L27 (
           22704) SEA FILE=EMBASE ABB=ON PLU=ON (SEXUAL DYSFUNCTION? OR SEXUAL
           4167) SEA FILE=WPIDS ABB=ON PLU=ON (SEXUAL DYSFUNCTION? OR SEXUAL D
L28 (
L29 (
           63399) SEA (SEXUAL DYSFUNCTION? OR SEXUAL DISFUNCTION? OR ERECTILE DYS
         255) SEA FILE=MEDLINE ABB=ON PLU=ON (FEMALE SEXUAL DYSFUNCTION? OR
L30 (
L31 (
            177) SEA FILE=BIOSIS ABB=ON PLU=ON (FEMALE SEXUAL DYSFUNCTION? OR
L32 (
            200) SEA FILE=CAPLUS ABB=ON PLU=ON (FEMALE SEXUAL DYSFUNCTION? OR
L33 (
           692) SEA FILE=EMBASE ABB=ON PLU=ON (FEMALE SEXUAL DYSFUNCTION? OR
L34 (
         334) SEA FILE=WPIDS ABB=ON PLU=ON (FEMALE SEXUAL DYSFUNCTION? OR F 1658) SEA (FEMALE SEXUAL DYSFUNCTION? OR FEMALE SEXUAL DISFUNCTION? O 112) SEA FILE=MEDLINE ABB=ON PLU=ON BENZIMIDAZOLINONE? OR "1-ETHYL
            334) SEA FILE-WPIDS ABB-ON PLU-ON (FEMALE SEXUAL DYSFUNCTION? OR F
L35 (
L36 (
L37 (
            159) SEA FILE-BIOSIS ABB-ON PLU-ON BENZIMIDAZOLINONE? OR "1-ETHYL-
L38 (
            609) SEA FILE=CAPLUS ABB=ON PLU=ON BENZIMIDAZOLINONE? OR "1-ETHYL-
L39 (
            135) SEA FILE=EMBASE ABB=ON PLU=ON BENZIMIDAZOLINONE? OR "1-ETHYL-
L40 (
            66) SEA FILE=WPIDS ABB=ON PLU=ON BENZIMIDAZOLINONE? OR "1-ETHYL-2
L41 (
           1081) SEA BENZIMIDAZOLINONE? OR "1-ETHYL-2-BENZIMIDAZOLINONE" OR "EBI
L42 (
           18992) SEA FILE=MEDLINE ABB=ON PLU=ON L24 OR L30
L43 (
           12810) SEA FILE=BIOSIS ABB=ON PLU=ON L25 OR L31
L44 (
           4748) SEA FILE=CAPLUS ABB=ON PLU=ON L26 OR L32
L45 (
           22707) SEA FILE=EMBASE ABB=ON PLU=ON L27 OR L33
L46 (
           4173) SEA FILE=WPIDS ABB=ON PLU=ON L28 OR L34
L47 (
           63430) SEA L29 OR L35
L48 (
           89255)SEA FILE=MEDLINE ABB=ON PLU=ON CLITOR? OR GENITAL? OR SEXUAL
L49 (
           54070) SEA FILE=BIOSIS ABB=ON PLU=ON CLITOR? OR GENITAL? OR SEXUAL G
          12575) SEA FILE=CAPLUS ABB=ON PLU=ON CLITOR? OR GENITAL? OR SEXUAL G 182062) SEA FILE=EMBASE ABB=ON PLU=ON CLITOR? OR GENITAL? OR SEXUAL G
L50 (
L51 (
L52 (
           5255) SEA FILE=WPIDS ABB=ON PLU=ON CLITOR? OR GENITAL? OR SEXUAL GE
L53 (
          343217) SEA CLITOR? OR GENITAL? OR SEXUAL GENITAL? OR PENIS? OR PENILE?
L54 (
          99793) SEA FILE=MEDLINE ABB=ON PLU=ON L42 OR L48
L55 (
           61673) SEA FILE=BIOSIS ABB=ON PLU=ON L43 OR L49
L56 (
           15359) SEA FILE=CAPLUS ABB=ON PLU=ON L44 OR L50
L57 (
          195622) SEA FILE=EMBASE ABB=ON PLU=ON L45 OR L51
L58 (
            8559) SEA FILE=WPIDS ABB=ON PLU=ON L46 OR L52
L59 (
          381006) SEA L47 OR L53
L60 (
               1) SEA FILE=MEDLINE ABB=ON PLU=ON L54 AND (L18 OR L36)
L61 (
                1) SEA FILE=BIOSIS ABB=ON PLU=ON L55 AND (L19 OR L37)
               3)SEA FILE=CAPLUS ABB=ON PLU=ON L56 AND (L20 OR L38)
2)SEA FILE=EMBASE ABB=ON PLU=ON L57 AND (L21 OR L39)
L62 (
L63 (
               3) SEA FILE=WPIDS ABB=ON PLU=ON L58 AND (L22 OR L40)
L64 (
L65 (
              10) SEA L59 AND (L23 OR L41)
L66 (
               6) DUP REM L65 (4 DUPLICATES REMOVED)
            731) SEA FILE=MEDLINE ABB=ON PLU=ON ((INTERMEDIATE CONDUCTANCE) (5
L67 (
           1070)SEA FILE=BIOSIS ABB=ON PLU=ON ((INTERMEDIATE CONDUCTANCE) (5A 1359)SEA FILE=CAPLUS ABB=ON PLU=ON ((INTERMEDIATE CONDUCTANCE) (5A 220)SEA FILE=EMBASE ABB=ON PLU=ON ((INTERMEDIATE CONDUCTANCE) (5A 51)SEA FILE=WPIDS ABB=ON PLU=ON ((INTERMEDIATE CONDUCTANCE) (5A)
L68 (
L69 (
L70 (
L71 (
L72 (
            3431) SEA ((INTERMEDIATE CONDUCTANCE) (5A) (CALCIUM? OR POTASSIUM?))
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L73 (
           821) SEA FILE=MEDLINE ABB=ON PLU=ON L18 OR L36 OR L67
L74 (
          1194) SEA FILE=BIOSIS ABB=ON PLU=ON L19 OR L37 OR L68
L75 (
         1935) SEA FILE=CAPLUS ABB=ON PLU=ON L20 OR L38 OR L69
L76 (
           347) SEA FILE=EMBASE ABB=ON PLU=ON L21 OR L39 OR L70
L77 (
           114) SEA FILE=WPIDS ABB=ON PLU=ON L22 OR L40 OR L71
         4411) SEA L23 OR L41 OR L72
L78 (
L79 (
            8) SEA FILE=MEDLINE ABB=ON PLU=ON L54 AND L73
L80 (
             7) SEA FILE=BIOSIS ABB=ON PLU=ON L55 AND L74
           12) SEA FILE=CAPLUS ABB=ON PLU=ON L56 AND L75
L81 (
L82 (
             2) SEA FILE=EMBASE ABB=ON PLU=ON L57 AND L76
L83 (
             3)SEA FILE=WPIDS ABB=ON PLU=ON L58 AND L77
L84 (
            32) SEA L59 AND L78
L85 (
            20) DUP REM L84 (12 DUPLICATES REMOVED)
L86 (
           141) SEA FILE=CAPLUS ABB=ON PLU=ON (INTERMEDIATE CONDUCTANCE CALCI
          609) SEA FILE=CAPLUS ABB=ON PLU=ON BENZIMIDAZOLINONE? OR "1-ETHYL-
L87 (
         1637) SEA FILE=CAPLUS ABB=ON PLU=ON ((INTERMEDIATE CONDUCTANCE) (5A
L88 (
         2210) SEA FILE=CAPLUS ABB=ON PLU=ON L86 OR L87 OR L88
L89 (
L90
                STR
         13897) SEA FILE=REGISTRY SSS FUL L90
L91 (
L92 (
          6484) SEA FILE=CAPLUS ABB=ON PLU=ON L91
          194) SEA FILE=CAPLUS ABB=ON PLU=ON L89 AND L92
L93 (
            0) SEA FILE=CAPLUS ABB=ON PLU=ON L93 AND (L26 OR L32 OR L50)
            0) SEA FILE=CAPLUS ABB=ON PLU=ON L93 AND (SEX? DYSF?)
L95 (
             2) SEA FILE=CAPLUS ABB=ON PLU=ON L93 AND (SEXUAL DYSFUNCTION? OR
L96 (
           20) SEA FILE=CAPLUS ABB=ON PLU=ON L92 AND (L26 OR L32 OR L50)
L97 (
L98 (
            6) SEA FILE=CAPLUS L85
L99 (
            20) SEA FILE=CAPLUS L97 NOT L98
     FILE 'REGISTRY' ENTERED AT 12:58:26 ON 14 APR 2005
L100
           50 S L90
L101
          13897 S L90 FULL
     FILE 'CAPLUS' ENTERED AT 12:58:47 ON 14 APR 2005
L102
           6484 S L101
L103
           2 S L102 AND (SEXUAL DESIRE? OR SEXUAL AROUSAL? OR ORGASM? OR SEX
  FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' ENTERED AT 12:59:35 ON 14
          21870 S (NICORANDIL? OR PINACIDIL? OR CROMAKALIM? OR MINOXIDIL? OR AP
L105
             16 S L104 AND (INTERMEDIATE CONDUCTANCE OR "IKCA" OR "IKCA(2+)")
L106
              5 DUP REM L105 (11 DUPLICATES REMOVED)
=> d cost.
COST IN U.S. DOLLARS
                                                SINCE FILE
                                                               TOTAL
                                                    ENTRY
                                                              SESSION
CONNECT CHARGES
                                                     10.64
                                                               12.72
NETWORK CHARGES
                                                     0.36
                                                                0.72
SEARCH CHARGES
                                                     20.79
                                                              198.70
DISPLAY CHARGES
                                                     1.10
                                                               6.40
                                                   _____
FULL ESTIMATED COST
                                                     32.89
                                                              218.54
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)
                                                SINCE FILE
                                                               TOTAL
                                                    ENTRY
                                                              SESSION
CA SUBSCRIBER PRICE
                                                               -1.46
                                                     0.00
IN FILE 'MEDLINE, BIOSIS, CAPLUS, EMBASE, WPIDS' AT 13:03:10 ON 14 APR 2005
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